

UNIVERSITY OF EDINBURGH

APPLICATIONS OF INFRARED SPECTROSCOPY

TO PHYSICO-CHEMICAL PROBLEMS

by

TO MY

PARENTS

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THESIS

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INTRODUCTION

During recent years some important developments and improvements have been made in the determination of organic functional groups. The need for accurate methods in functional group analysis is an obvious one, and the most favoured procedures are those which combine the highest accuracy with the criteria of simplicity and reliability. The first functional group analysis of the alkoxy determination was developed by David 10 years ago.

PART I

APPLICATIONS OF INFRARED SPECTROSCOPY  
TO THE ALKOXYL DETERMINATION

The apparent basic simplicity of the alkoxy determination is somewhat offset by the rigorous experimental control demanded, and it has become one of the simplest, most compact, and rapid of functional group determinations. For attainment of the highest accuracy, it is necessary that: a) the alkyl compound is rendered soluble in the reaction mixture by means of suitable reagents; b) traces of iodine and hydroiodic acid vapours are not permitted to reach the absorber; and c) volatile reaction products which may react with silver halides in the absorber are completely removed. Special in the substituting agent most generally employed, and, in order to fulfil items b) and c), a chamber is placed between the reaction vessel and the absorber. An inert carrier gas, nitrogen or carbon dioxide, is

### INTRODUCTION

During recent years some important developments and improvements have been made in the determination of organic functional groups. The need for accurate methods in functional group analysis is an obvious one, and the most favoured procedures are those which combine the highest accuracy with the criteria of rapidity and reliability. The first functional group analysis -- the alkoxy determination -- was developed by Zeisel 76 years ago, and has been the subject of considerable attention by analysts ever since. This reflects the continuing importance of the method in the analysis of naturally occurring substances.

With very few exceptions, all the methods for the alkoxy determination are based on the classical Zeisel reaction,<sup>1</sup> involving cleavage of the ether linkage with boiling hydriodic acid. An alkyl iodide is liberated and subsequently absorbed and determined either gravimetrically,<sup>1</sup> or iodometrically by the Viebock-Schwappach procedure.<sup>2</sup>

The apparent basic simplicity of the alkoxy determination is somewhat offset by the rigorous experimental control demanded, but it still remains one of the simplest, most compact, and rapid of functional group determinations. For attainment of the highest accuracy, it is necessary that a) the alkoxy compound is rendered soluble in the reaction mixture to ensure complete reaction; b) traces of iodine and hydriodic acid vapours are not permitted to reach the absorber; and c) volatile reaction products which may react with alkyl iodides in the absorber are completely removed. Phenol is the solubilising agent most generally employed, and, in order to fulfil cases b) and c), a scrubber is placed between the reaction vessel and the absorber. An inert carrier gas, nitrogen or carbon dioxide, is

employed to sweep over liberated alkyl iodides. The apparatus, therefore, consists of a reaction vessel with an inlet-tube for the carrier gas, a condenser to minimise volatilisation of hydriodic acid and iodine vapours, a scrubber, and an absorber.

Apparatus. Pregl's apparatus<sup>5</sup> has for many years been the accepted design in Britain, and a slightly modified apparatus is now accepted as the British standard; this is described fully in B.S. 1428: Part C1, 1954. The apparatus consists of a combined reaction flask and water condenser connected by suitable ground-glass joints to a spiral gas scrubber and delivery tube which is led into a receiving vessel. Many individual variants on this design have been proposed to comply with the particular conditions desired for the determinations in question. (See, for example, refs. 4 and 5).

An apparatus for the sub-micro determination of alkoxy groups has been described by Belcher, Bhatta and West,<sup>6</sup> and resembles a scaled-down version of the British standard.

Hydriodic Acid. Hydrogen iodide forms an azeotrope with water which contains 57% HI, has a specific gravity of 1.70 and boils at 127°C. This strength of acid is almost universally employed in alkoxy determinations, although the use of acid of specific gravity 1.96 has been advocated<sup>7</sup> for compounds containing more than two alkoxy groups despite the increased difficulties involved. Elek<sup>8</sup> proposed the addition of a few drops of the more concentrated acid, after phenol had been added as a solubilising agent, to maintain the strength of the azeotrope.

For work of the greatest accuracy, the purity of the acid must be high. A few firms make hydriodic acid of micro-analytical reagent purity, but some analysts prefer their own preparations, and several detailed procedures have been described.<sup>9,10</sup>

Due to the strong reducing nature of hydriodic acid, a sample, on exposure to air and with increasing use, becomes steadily darker in colour unless suitable precautions are taken. There has been much controversy over the colour of the acid and the accuracy thereby attained. Some authors maintain that the use of fresh, colourless acid is essential and add hypophosphorous acid to ensure this; others maintain that the colour of the acid is unimportant provided it is refluxed well before use. When the acid is very dark, it is generally agreed that the danger of iodine volatilisation merits its disuse.

Solubilisers and Solubilising Techniques. The most commonly used solubilising agents are phenol<sup>11</sup> and phenol/propionic anhydride<sup>4,12</sup> admixtures, but acetic anhydride,<sup>13</sup> propionic anhydride,<sup>14</sup> phthalic anhydride and carbon tetrachloride<sup>15</sup> have also been proposed. The numerous solubilising procedures to be found in the literature are based on one or other of two techniques: either, a) the weighed sample is added to a reaction mixture rich in the solubilising agent, or b) the sample is completely dissolved in the agent before the addition of hydriodic acid. Elek,<sup>8</sup> who used the latter technique, suggested that for the best results, the dissolution process should extend over a period of half-an-hour.

The quantities of solubilising agents used by different analysts vary considerably, and depend on the technique employed. If the weighed sample to be analysed is added directly to the reaction mixture, the latter contains a high proportion of the solubilising agent, (Kirsten and Ehrlich-Rogozinsky<sup>4</sup> use 60g. phenol, 2g. red phosphorus, 5ml. propionic anhydride per 100g. hydriodic acid, and Heron *et al.*<sup>16</sup> use 2.5g. phenol per 5ml. ampoule of hydriodic acid). If the sample is dissolved prior to the addition of the acid, a few crystals of phenol are generally regarded as being adequate.

In addition to the general techniques outlined above, several workers have found that specific solubilising procedures are required for certain compounds. Thus Neumann<sup>17</sup> describes a procedure to be followed for highly methylated carbohydrates, and Mayer<sup>18</sup> describes a series of compounds which require a large excess of phenol to be present before correct analyses are achieved.

Carrier Gas. Nitrogen or carbon dioxide are used as inert carrier gases. Optimum flow-rates depend on apparatus design but most analysts prefer a slow flow-rate of between 4 and 8 ml./min. Inglis,<sup>5</sup> however, considered that a flow-rate of 12 - 15 ml./min. was desirable to overcome the solubility of methyl iodide in aqueous scrubbing solutions.

Duration of Analysis and Temperature of Condenser Water. For methoxyl estimations, a reaction period of  $\frac{3}{4}$  to 1 hr. is usually employed, and a slightly longer period allowed for ethoxyl estimations. In both cases cold condenser water is used except where certain investigators prefer the use of an air condenser. However, Belcher *et al.*<sup>12</sup> maintained that for satisfactory ethoxyl estimations a reaction period of  $1\frac{1}{2}$  hr. was required with the condenser shut off for the last  $\frac{1}{2}$  hr. In the rare case when it has been desired to estimate butoxyl,<sup>19</sup> a reaction time of 3 hr. has been allowed with hot water flowing through the condenser.

Inglis,<sup>5</sup> on the other hand, has shown that reaction with hydriodic acid at 127°C. is extremely rapid, and that, using a flow-rate of 15 ml./min. of carbon dioxide, quantitative yields of methyl and ethyl iodides are obtained from vanillin and phenacetin respectively in  $7\frac{1}{2}$  min. using cold condenser water.

Kirsten and Ehrlich-Rogozinsky<sup>4</sup> required distillation times of 12 and 22 min. using a nitrogen flow-rate of 25 ml./min. for the same two iodides.

Wash Liquids. A measure of the importance assigned to the alkoxyl determination

is very well reflected in the intensive investigations which have been carried out concerning the suitability and efficiency of different wash liquids. The aim has always been an increased accuracy in the results obtained, and to this end at least 14 different wash liquids have so far been proposed.

The main impurities which can be carried over from the reaction vessel are hydrogen iodide, free iodine, and hydrogen sulphide (from sulphur-containing compounds). These will vitiate results if allowed to reach the absorber. The original analytical procedure of Zeisel,<sup>1</sup> developed as an aid to the elucidation of alkaloid structures, used an aqueous suspension of red phosphorus at 50 - 60°C. as wash liquid. Analysts were quick to point out, however, that such a wash liquid was inadequate for sulphur-containing compounds, and Bamberger and Benedikt<sup>20</sup> advocated the use of a red phosphorus suspension in 10% aqueous cadmium iodide in such cases.

The great majority of alkoxy determinations are on sulphur-free compounds, and as a general wash liquid Friedrich<sup>21</sup> proposed 3% aqueous sodium thiosulphate. This was commonly used, but more recent work, particularly by Franzen et al.,<sup>22</sup> has shown that the use of thiosulphate is decidedly detrimental, and it was shown at the turn of the century that methyl iodide reacts with aqueous sodium thiosulphate to form sodium methyl thiosulphate.<sup>23</sup> (Friedrich actually found<sup>21</sup> that a calculable positive correction was necessary in all his alkoxy results, but attributed this to incomplete reaction with his precipitant, silver nitrate, in the absorber). Nevertheless, although the use of thiosulphate appears ill-advised, some workers prefer its use in admixture with other salts; in particular, a 5% aqueous cadmium sulphate/5% aqueous sodium thiosulphate solution has been highly recommended,<sup>5,10,24</sup> while others proposed include sodium thiosulphate/sodium chloride<sup>24</sup>

and sodium thiosulphate/cadmium sulphate/red phosphorus.<sup>25</sup>

Stritar<sup>26</sup> first proposed aqueous sodium antimonyl tartrate as an efficient wash liquid, and more recently Franzen et al.,<sup>22</sup> Belcher et al.,<sup>6,12</sup> and Bethge and Carlson<sup>27</sup> have all found the use of a 10% solution excellent both in the presence and absence of sulphur. Franzen et al.<sup>22</sup> have also proposed that 5% aqueous solutions of hydroxylamine hydrochloride, sodium carbonate and L-ascorbic acid all act as efficient wash liquids.

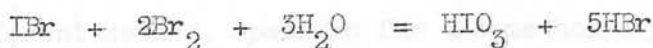
Heron et al.<sup>16</sup> in a recent critical investigation have shown that water alone is an efficient wash liquid, particularly at the boiling point of methyl iodide, 42°C. (At least one other worker<sup>28</sup> had previously found its use successful). They found the most efficient general wash liquid, however, to be a 25% aqueous solution of sodium acetate. Kirsten and Ehrlich-Rogozinsky,<sup>4</sup> and Gran<sup>29</sup> have used aqueous sodium bicarbonate solutions, in the absence of sulphur.

By far the best critical survey of wash liquids has been carried out recently by Bethge and Carlson.<sup>27</sup> In the absence of sulphur, the choice of wash liquid (except for those containing thiosulphate) appeared to be non-critical, and distilled water, dilute hydrochloric acid, sodium bicarbonate, sodium antimonyl tartrate or cadmium sulphate solutions all acted equally well. When sulphur compounds are present, however, there is the possibility of interaction between the liberated hydrogen sulphide and alkyl iodide leading to mercaptan formation, a reaction favoured by alkaline conditions. Consequently, solutions of sodium bicarbonate and sodium acetate should not be used as wash liquids. Under such conditions the most satisfactory reagents were sodium antimonyl tartrate and cadmium sulphate, the latter being more efficient when large amounts of sulphur were present. An aqueous solution of cadmium sulphate was first proposed as an efficient wash liquid in the presence

of sulphur in 1915, by Kirpal and Bthn.<sup>50</sup>

Solid Scrubbers. The use of solid scrubbers in place of aqueous wash liquids was investigated by Fierz-David et al.<sup>51</sup> in 1945, primarily for the determination of alkimide groups. In spite of their immediately obvious advantages of higher efficiency and greater ease of handling, the possibility of their application to routine alkoxy determinations has been neglected until very recently. Fierz-David et al. favoured the use of a scrubber composed of 75% soda asbestos : 25% calcium chloride, the latter being present to remove any distilling or liberated water vapour. Filipović and Stefanac<sup>52</sup> have demonstrated that soda asbestos quantitatively absorbs iodine, hydrogen iodide and hydrogen sulphide vapours, and that, with its use, flow rates of carrier gas are non-critical. The accuracy of their results were equal to those obtained when wash liquids were used. However, Večeřa and Spěvák<sup>53</sup> found the use of soda asbestos unacceptable and prepared a dry scrubber of sodium antimonyl tartrate on Kieselgur, dried at 60°C.

Methods of Estimation. The original method of estimation<sup>1</sup> depended on the quantitative precipitation of silver iodide when the liberated alkyl<sup>^</sup> was absorbed in an alcoholic solution of silver nitrate. Although this procedure has been considerably improved since its inception and is still used by some analysts, particularly Steyermark,<sup>34</sup> it has largely been superceded by the titrimetric method based on investigations by Leipert<sup>35</sup> and developed by Viebock, Schwappach and Brecher.<sup>2</sup> This has remained unchanged to date and consists of absorbing the liberated alkyl iodide in a potassium acetate/glacial acetic acid solution containing some bromine, which causes iodate to be quantitatively formed. After discharging excess bromine with formic acid, potassium iodide is added and the liberated iodine titrated with standard thiosulphate solution using starch indicator. The reactions involved:



show that, by this procedure, there is an enhancement factor of six, six atoms of iodine being released for every molecule of alkyl iodide originally present. A high accuracy can therefore be achieved. However, for every determination a "blank" run has to be performed to allow for traces of undesirable volatile products reaching the absorber and for traces of iodine in the bromine used. The "blank" titre is deducted from the actual titre found.

#### Selective Methoxyl Determinations and Simultaneous Alkoxy Determinations. Neither

of the above two methods, which both depend only on the determination of liberated iodine, can differentiate when more than one type of alkoxy group is present in the sample being analysed. A selective determination is required which will discriminate between different alkyl radicals.

Several methods have been evolved for the selective determination of methoxyl. Feist<sup>56</sup> proposed the use of an alcoholic solution of dimethylaniline as an absorber. Methyl iodide is quantitatively absorbed and trimethyl phenyl ammonium iodide formed in almost theoretical yield, higher alkyl iodides reacting so slowly that they cause no interference. In a reinvestigation, Willstätter and Utzinger<sup>37</sup> preferred the use of excess trimethylamine in absolute ethanol, because of its higher rate of reaction and greater specificity. Gran<sup>58</sup> has improved this latter method by using an isopropanolic solution of trimethylamine as absorbent for methyl iodide; precipitation of the symmetrical quaternary salt is quantitative. Kirpal and Böhn,<sup>50</sup> on the other hand, favoured the use of pyridine as an absorbent. Methyl iodide is absorbed and reacted quantitatively, while other alkyl iodides are only slightly

absorbed or react only very slowly. Mathers and Pro<sup>39</sup> have recently described a completely different method, specific for the methoxyl group, which involves hydrolysis of the compound with concentrated sulphuric acid followed by distillation of the liberated methanol. This is oxidised to formaldehyde which is then condensed with chromotropic acid and determined spectrophotometrically.

The simultaneous determination of alkoxy groups creates considerable difficulties and the different methods evolved suffer from being very lengthy. For the simultaneous determination of methoxyl and ethoxyl Cooke and Hibbert<sup>40</sup> first determined the total alkoxy content by the Viebock method, and then the methoxyl content by Gran's method<sup>38</sup> above. Friedrich<sup>41</sup> used a completely different technique. An alkoxy determination was first made by the customary Zeisel method. A second sample was then treated with the hydriodic acid reaction mixture, but the distilling alkyl iodides were combusted to form iodine, water and carbon dioxide. The last-named was gravimetrically determined. In the first determination the total alkoxy content was found, and in the second the total number of gram atoms of carbon in the alkoxy groups. The method thus distinguished between various possible alkoxy groups, and, when only two different groups were present in the sample, permitted their individual estimation. The Friedrich method is the only method known to date which can be used for the simultaneous determination of alkoxy groups not including methoxyl. Recent modifications of the method have been described by Filipović and Štefanac,<sup>32</sup> and by Fukuda and Sai.<sup>42</sup>

Conclusions. It will be clear from the foregoing review that, at the present time, no absolutely standard method for the determination of alkoxy groups exists, and that many procedures are individual to the analyst concerned. A critical survey of each individual stage in the determination would be advantageous in reducing

the number of possible variants to a minimum, and in presenting the combination best enabling the highest accuracy to be achieved, under the most variable chemical conditions.

A recently developed sensitive infrared technique<sup>43,44</sup> for the quantitative determination of substances in the vapour phase offered a splendid opportunity of carrying out such a survey. Milligram quantities of alkyl iodides can be quantitatively trapped in liquid nitrogen and can subsequently be determined by referring the heights of selected characteristic peaks in their infrared spectrum to a carefully constructed calibration curve. The latter is previously obtained under carefully standardised spectroscopic conditions by quantitatively volatilising weighed amounts of purified alkyl iodides into the infrared gas-cell.

By isolating and examining the volatile reaction products at various junctures of the alkoxyl apparatus, sources of loss of alkyl iodides could be traced, and the effects of many of the differing experimental techniques critically examined in situ. The greatest single advantage offered by infrared spectroscopy in such a survey lies in the ability of the experimenter to study all volatile reaction products directly as spectra. Any indirect method of assay, whether gravimetric or titrimetric, cannot elucidate the nature or source of any interfering substance, since in producing the interference the substance is necessarily destroyed. Unless reaction occurs in the vapour phase between an alkyl iodide and another volatile reaction product, no interference will be encountered using the infrared method, except in the case where the spectrum of a volatile product overlaps the particular alkyl iodide peaks used for estimation.

EXPERIMENTAL

Apparatus. The apparatus developed is shown in Fig. 1. It consists of a combined reaction-flask and water condenser (as described in B.S. 1428: part C1, 1954 (type 2 apparatus)), a delivery tube, and a trap<sup>45</sup> with Vigreux-type indentations in the inner absorption tube. Since it is necessary in infrared spectroscopy to exclude water vapour, the delivery tube was packed with a little anhydrone, and an anhydrone guard-tube was fitted to the exit of the trap, as shown in Fig. 1. Preliminary tests revealed that, of the normal volatile reaction products, anhydrone retained only water vapour. In critical investigations on wash liquids, a spiral scrubber (B.S. 1428: part C1, 1954 (type 2 apparatus)) was interposed between the condenser and the trap.

Reagents.

Hydriodic Acid	--	M.A.R., specific gravity 1.70, (6ml. ampoules)
Phenol	--	AnalaR
Anhydrone	--	M.A.R., 14 - 22 mesh
Soda Asbestos	--	M.A.R.
Nitrogen	--	"N.O.F." grade; used as carrier gas
Alkyl iodides	--	for calibration purposes, the reagent grade was distilled three times; the still-head was packed with anhydrone, and the middle fraction collected each time. The liquids were stored in light-proof bottles with ground-glass stoppers.

Infrared Gas-cells. Two gas-cells<sup>44</sup> were used. One, of length 12.5cm. and internal volume 58.0c.c., permitted determination of 4 - 10 mg. quantities of alkyl iodides; the other, 31.5 cm. long and 51.5 c.c. internal volume, permitted determinations in

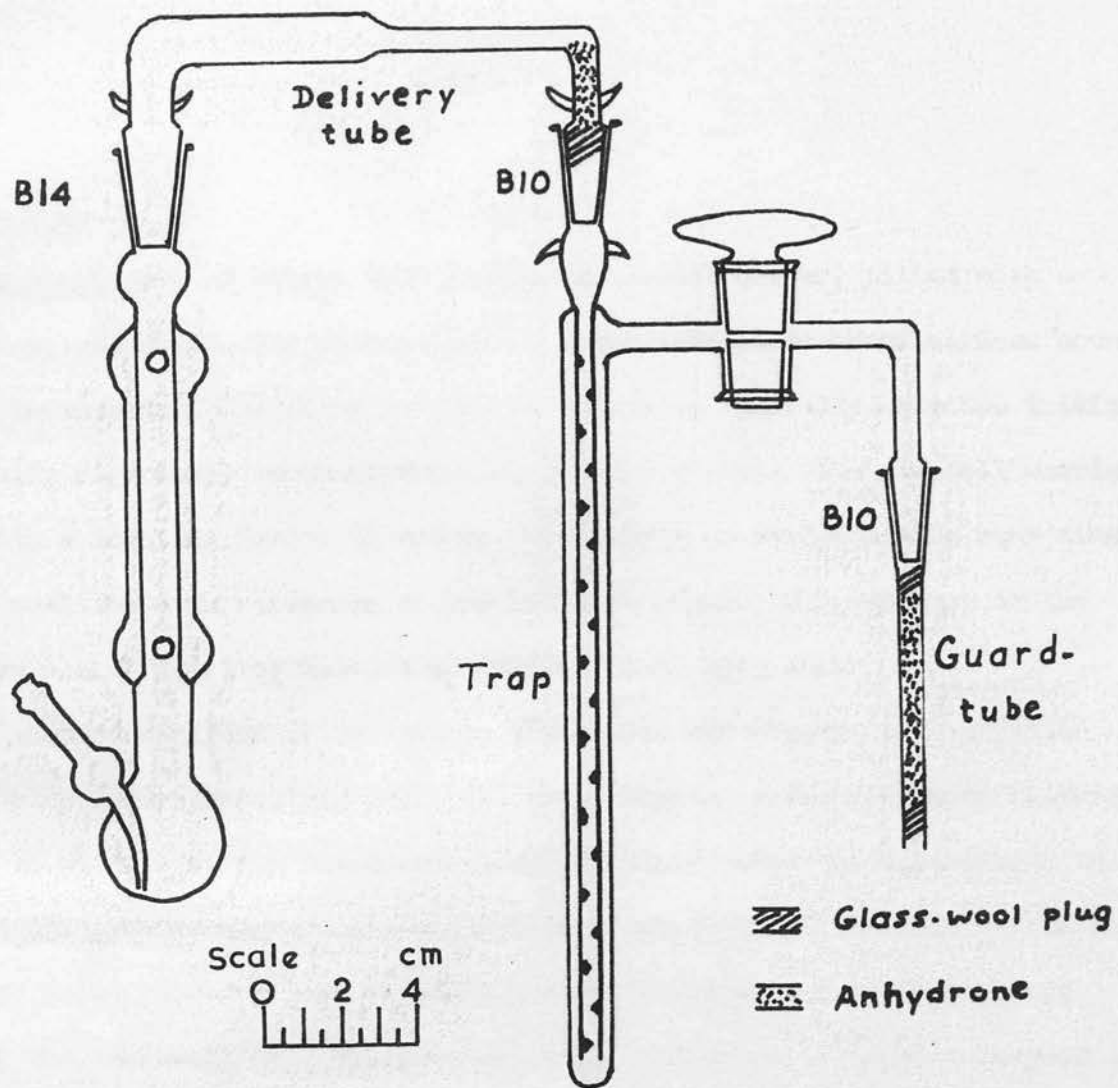


Fig. 1. Assembled Alkoxy Apparatus.

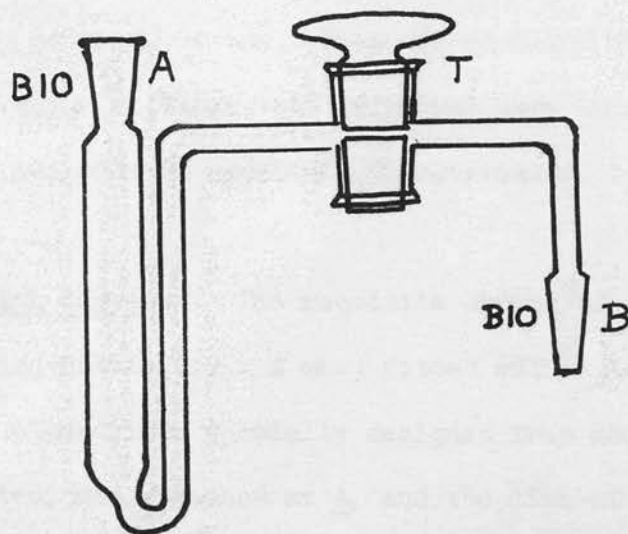


Fig. 1A. Calibration Trap.

the range 1 - 4 mg.

Infrared Measurements. A Hilger H800 double-beam spectrometer, fitted with a rock-salt prism, was used. For estimations of alkyl iodides to be of maximum accuracy, the standard instrumental operating conditions had to be carefully selected initially and subsequently rigorously controlled during determinations. The gas-cell carrier was fitted with a locating device to ensure replacement of the gas-cells each time in identical position with reference to the infrared beams. Compensation in the reference beam was effected by matched gas-cells filled with air.

Reproducibility of percentage absorption for a given concentration depends on the recorder zero stability; all peak heights, therefore, were measured with respect to an arbitrarily fixed base-line associated with the wave-length involved. With all spectrometer conditions constant, small local fluctuations in the base-line were found to occur, due to small energy losses caused by fogging and scratching of the rock-salt cell windows, which had therefore to be kept in good condition. Such fluctuations could be satisfactorily compensated by adjustment of an iris diaphragm located in the reference beam.

Weighing of Samples. The spectrometer recorded percentage absorption to an accuracy of  $\pm 0.5\%$ . This fixed the accuracy of the method and obviated the necessity of using a microbalance. By adjustment of tares, all weighings were made within the range of the 0 - 50 mg. graticule scale of an aperiodic direct-reading balance having an accuracy of  $\pm 10 \mu\text{g}$ .

Construction of Calibration Curves. The requisite amount of alkyl iodide was weighed in a micro weighing-bottle (12 x 4 mm.) fitted with a leak-proof ground-glass stopper. The bottle was placed in a specially designed trap shown in Fig. 1A. The correct gas-cell, evacuated, was attached at A, and the limb of the trap immersed

in liquid nitrogen. B was connected to a suitable vacuum-line<sup>45</sup> and the system evacuated, the trap still being immersed in the coolant. Tap T was closed and the system removed from the vacuum-line. The coolant was removed and the trap allowed to reach room temperature, then warmed gently over a hot-plate. This caused the release of the weighing-bottle stopper and volatilisation of the alkyl iodide. With an anhydrous guard-tube attached to B, T was slowly opened and air allowed to sweep through the trap into the cell. By this technique, quantitative <sup>transfer</sup> of the alkyl iodide to the cell, within the experimental limits of  $\pm 1\%$ , was easily achieved. Bringing the cell up to atmospheric pressure standardised any "pressure broadening" effects<sup>45</sup> which might occur. Day to day variations in pressure had no detectable effect.

The particular absorption peak selected for calibration was then drawn five to eight times. This minimised any error caused by the pen recorder, the reproducibility of which was 0.25%. The mean peak height was then calculated. It was found that, at the partial pressures used, peak heights were very sensitive to small changes in concentration and were, under standard conditions, very easily measured. Calibration curves were therefore constructed with reference to peak heights. Fig. 2 shows a series of typical curves obtained using the more sensitive gas-cell. The positions (in  $\text{cm.}^{-1}$ ) of the particular alkyl iodide absorption peaks selected for calibration, and on which all determinations were based, are as follows:

methyl iodide	1264 $\text{cm.}^{-1}$
ethyl iodide	1216 $\text{cm.}^{-1}$
n-propyl iodide	1199 $\text{cm.}^{-1}$
n-butyl iodide	1196 $\text{cm.}^{-1}$

Efficiency of Trapping. Various weights of alkyl iodides were added to the reaction

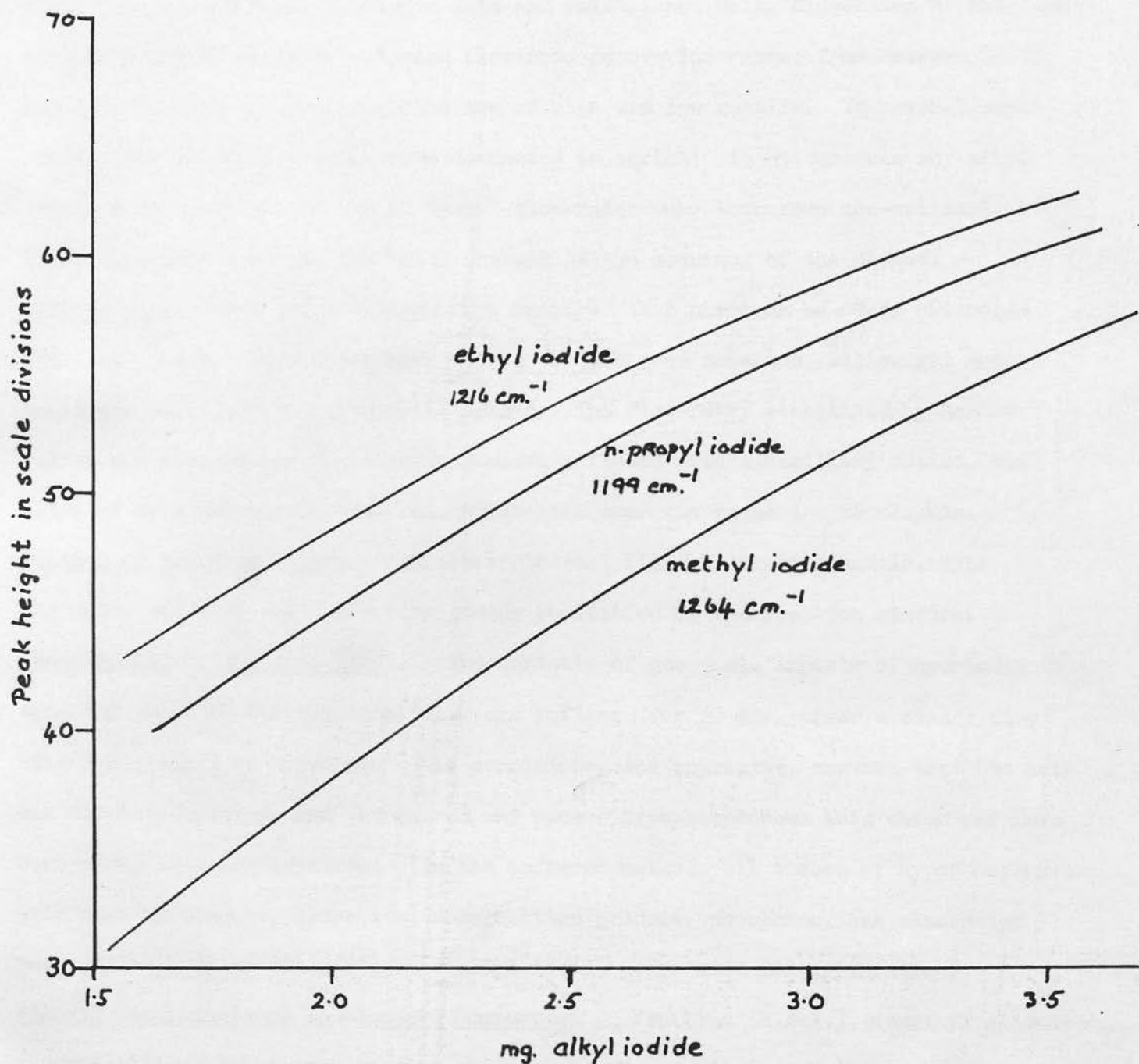


Fig. 2. Calibration Curves for more sensitive gas-cell.

flask filled with 6 ml. hydriodic acid and volatilised using flow-rates of nitrogen between 4 and 20 ml./min. At each flow-rate recoveries ranged from between 99.0% and 101.0%, with an equal distribution of high and low results. In several experiments, two absorption traps were connected in series; in no case was any alkyl iodide detectable in the second trap. Flow-rates were therefore non-critical. These experiments led to  $\pm 1\%$  being claimed as the accuracy of the method.

Carrier Gas. The infrared technique required that nitrogen be used. Nitrogen ("N.O.F." grade) was successively passed through soda asbestos, silica gel and anhydrous to effect complete purification. The flow-rate, stabilised by needle valves and passage through a large reservoir fitted with a capillary outlet, was adjusted by a Rotameter, Type 704, calibrated over the range 4 - 25 ml./min.

Heating of Reaction Flask. An electrothermal flexible heating mantle, Type MBJ 1822, was used, and gave very steady ebullition of the reaction mixture.

Conditioning of the Apparatus. The contents of one 6 ml. ampoule of hydriodic acid was added to the reaction flask and refluxed for 30 min. under a steady flow (6 - 8 ml./min.) of nitrogen. This conditioned the apparatus, ensured that the acid was constant-boiling, and decomposed any excess hypophosphorous acid which may have been added as a preservative. (In the infrared method, all traces of hypophosphorous acid must be removed, since its decomposition product, phosphine, has absorption peaks which overlap the particular alkyl iodide peaks used for calibration).

Alkoxy Determinations on Standard Compounds. Vanillin (M.A.R.),  $\alpha$ -methyl glucoside (recrystallised laboratory reagent grade), and phenacetin (M.A.R.) were used as standard alkoxy compounds. The following technique was found to be very successful. The sample was weighed in a long-handled weighing spoon.<sup>16</sup> 20 - 40 mg. phenol was then added to the spoon, which was warmed gently over a hot-plate to form a homogeneous

melt at as low a temperature as possible. The spoon was placed in the reaction flask to which 6 ml. hydriodic acid had been added, conditioned and cooled. The delivery tube, packed with fresh anhydrone, was attached to a clean trap fitted with an anhydrone guard-tube, and the trap immersed in liquid nitrogen. The delivery tube was quickly connected to the reaction condenser, so assembling the apparatus as in Fig. 1. Ground-glass joints were lightly coated with silicone grease. (No scrubber is required using the infrared method, since the most common vapours released from the reaction mixture, hydrogen iodide, iodine and hydrogen sulphide, do not interfere with the determination. There is no reaction between these and alkyl iodides in the vapour phase, and no overlapping of peaks in their infrared spectra occurs). The nitrogen flow-rate was adjusted to 6 - 8 ml./min., and the heating mantle switched on. After ebullition had commenced, 30 min. was permitted for methoxyl and ethoxyl estimations. The trap was then removed and stoppered, keeping it immersed in coolant. The trapped products were volatilised into the appropriate gas-cell by the method already described, and the spectrum of the products drawn. The characteristic alkyl iodide peak, on which calibration was based, was drawn about six times, and the average peak height calculated. Reference to the calibration curve gave the weight of alkyl iodide liberated.

Table 1 shows the results obtained for the above three standard compounds. This gives a true representation of the poorest results that may be expected, since none of the results obtained was rejected. The standard deviation is also shown.

TABLE 1

Results of Alkoxy Determinations on Standard Compounds

Compound	Range of sample weights taken, mg.	No. of detns.	% alkoxy		Stand. devn.	Max. divergence from theory	
			found	theory		+	-
Vanillin	1.84 - 3.59	15	20.39	20.40	0.16	0.28	0.28
$\alpha$ -methyl-D-glucoside	2.58 - 4.36	5	15.99	15.99	0.08*	0.11	0.07
Phenacetin	2.82 - 3.67	6	25.18	25.15	0.17*	0.20	0.23

\* Calculated by the range method.

To further test the general applicability of the method, a series of organic compounds containing a wide range of other functional groups were analysed as "unknowns," using a reflux period of 30 - 45 min. The results are shown in Table 2.

TABLE 2

Results of Alkoxy Determinations on Selected Compounds

Compound	Weight taken, mg.	% alkoxy	
		found	theory
		methoxyl	
Aceto-p-anisidide	3.22	18.7	18.8
Anisic acid	2.66	20.4	20.4
Anisonitrile	2.95	23.3	23.5
o-azoanisole	2.16	25.4	25.6
Bergenin hydrate	4.93	8.96	8.99
	4.20	9.06	

TABLE 2 (Continued)

Compound	Weight taken, mg.	% alkoxy	
		found	theory
Brucine	3.95	15.7	15.7
tert-butyl-p-hydroxyanisole	(4.61 3.13)	16.9 17.1	17.2
Colchicine	2.01	31.0	31.1
Deoxyanisoin	(2.46 2.31)	24.2 24.1	24.2
3:4-dimethoxybenzaldehyde	1.76	37.5	37.3
2:6-dimethoxyphenol	3.16	40.8	40.3
$\beta$ -2:3-di-O-methyl xylose	2.25	35.0	34.8
2:3-epoxypropyl-p-methoxyl phenyl ether	3.50	17.0	17.2
Gusathion*	7.72	19.4	19.6
Hydroquinone dimethyl ether	1.62	44.4	44.9
p-methoxyacetophenone	(2.59 2.48)	20.4 20.5	20.7
p-methoxyazobenzene	4.51	14.5	14.6
3-methoxybenzanthrone	5.40	11.9	11.9
4-methoxy-2:5-toluquinone	2.50	20.3	20.4
Methyl anisate	1.53	37.5	37.3
3-O-methyl glucose	2.73	16.1	16.0
$\beta$ -naphthyl methyl ether	2.31	19.6	19.6
Narcotine	2.04	22.7	22.5
Neo-hesperidin	16.80	5.05	5.09
p-nitroanisole	(2.30 2.92)	20.3 20.4	20.4
Papaverine sulphate	1.82	28.2	28.4
Quinine	8.01	9.56	9.57
2:3:4:6-tetramethylglucose	1.31	52.1	52.5
3:4:5-trimethoxybenzoic acid	1.63	44.1	43.9
3:4:5-trimethoxycinnamic acid	3.93	39.0	39.1

\* Gusathion: S-(1:2:3:4-tetrahydro-6-oxo-benzo-1:2:3-triazin-2-yl)-methyl-O-O-dimethyl-phosphorothiothionate.

TABLE 2 (Continued)

Compound	Weight taken, mg.	% alkoxy	
		found	theory
		ethoxyl	
2-ethoxy-1:6-dibromonaphthalene	(5.52 5.81)	13.7 13.5	13.7
Ethyl-β-ethoxycrotonate	1.80	57.0	57.0
2:4-diamino-4'-ethoxyazobenzene	4.28	17.5	17.6
p-diethoxybenzene	(1.41 1.58)	53.9 53.0	54.2
Pyridoxyl-ethyl-acetal hydrochloride	3.13	19.4	19.5

Having established that the reaction conditions described and the spectroscopic method of determining methyl and ethyl iodides gave satisfactory analyses of pure reference compounds, the following investigations were made.

It has been observed that the presence of free iodine in the reaction mixture was in fact advantageous. A yield of 91% ethoxyl acceptable results were obtained in the presence of 20 mg. ethyl iodide, although a slightly increased blank value was observed. Experiments performed by the infrared technique confirm that the acid colour has no effect on the yield of ethyl iodide. Slight volatilization of iodine may, however, occur from very dark mixtures, particularly if the compound under analysis contains sulphur or is a carbohydrate material. As Kirsten pointed out, this imposes an additional test on the efficiency of any scrubber, and may introduce a source of error.

Repeated Use of Acid in Routine Analysis. In routine analyses, many compounds are known to decompose quantitatively in the normal reaction time, one charge of acid can safely be used for 8 determinations (average sample weight 5 mg.) provided the mixture is replaced for 30 min. between each determination. In the series of experiments, 14 successive determinations were satisfactorily made without change

## INVESTIGATIONS

### 1. A Critical Examination of Some Aspects of the Alkoxy Determination.

Strength and Colour of Hydriodic Acid. The M.A.R. constant-boiling acid, conditioned as already described, was found to be satisfactory in all analyses reported in Tables 1 and 2. Tests showed that, at 6 - 8 ml./min., only trace amounts, if any, of hydriodic acid were volatilised. The use of more concentrated acid would give increased amounts of distilling acid vapour, so introducing a possible source of error. Furter<sup>25</sup> stated that the use of fresh, colourless acid was essential. Steyermark,<sup>34</sup> however, found that the colour was non-critical if the acid was refluxed before use. More recently, it has been observed that the presence of free iodine in the reaction mixture was in fact advantageous.<sup>46</sup> Belcher et al.<sup>12</sup> obtained acceptable results titrimetrically in the presence of 20 mg. added iodine, although a slightly increased blank value was observed. Experiments performed by the infra-red technique confirm that the acid colour has no effect on the yield of alkyl iodide. Slight volatilisation of iodine may, however, occur from very dark mixtures, particularly if the compound under analysis contains sulphur or is a carbohydrate material. As Kirsten pointed out,<sup>4</sup> this imposes an additional test on the efficiency of any scrubber, and may introduce a source of error.

Repeated Use of Acid in Routine Analyses. In routine analyses, when compounds are known to decompose quantitatively in the normal reaction time, one charge of acid can safely be used for 8 determinations (average sample weight 5 mg.) provided the mixture is refluxed for 30 min. between each determination. In one series of experiments, 14 successive determinations were satisfactorily made without change

of acid. Care must always be exercised, however: certain compounds which contain alkimide (N-alkyl) groups have been found to liberate alkyl iodides continuously for several hours on refluxing with hydriodic acid.<sup>47</sup> (Cf. 46).

Period of Reflux and Temperature of Condenser Water. Experiments were performed to find the rates of release of methyl, ethyl, n-propyl and n-butyl iodides from vanillin, phenacetin, 4-n-propoxy- and 4-n-butoxy-diphenyl, respectively. The flow-rate of carrier gas used was 6 - 8 ml./min. (i.e. that most generally used by analysts), and a fast flow of cold condenser water<sup>^</sup> (≈ 3 litre/min.). The results obtained are summarised in Fig. 3. Quantitative recovery of methyl iodide from vanillin was effected in 10 - 15 min., and of ethyl iodide from phenacetin in 15 - 20 min., from commencement of ebullition. n-propyl and n-butyl iodides were quantitatively recovered from 4-n-propoxy- and 4-n-butoxy-diphenyl in 45 min. and 60 min. respectively. These results vary little from those found by Kirsten<sup>4</sup> using a fast flow-rate of carrier gas of 25 ml./min. It is clear, therefore, that reaction with hydriodic acid at 127°C. is very rapid,<sup>5</sup> and that volatilisation times are short, even with use of a fast flow of cold condenser water.

The use of prolonged reaction times (e.g. 1½ hr. for ethoxyl,<sup>12</sup> 3 hr. for butoxyl with the use of hot condenser water<sup>19</sup>) is clearly unwarranted and needlessly time-consuming. The practice of shutting off the condenser water<sup>12</sup> or of using hot water<sup>19</sup> is also unnecessary, and may indeed be detrimental to the analysis due to increasing the possibility of volatilisation of iodine vapour which may bypass the scrubber and reach the absorber.

Determinations on Volatile Liquids. Earlier investigators have found that double distillation<sup>5,15,54</sup> or the use of a modified apparatus<sup>4,5</sup> was necessary for quantitative results. Using the infrared method, a technique has been evolved which gives

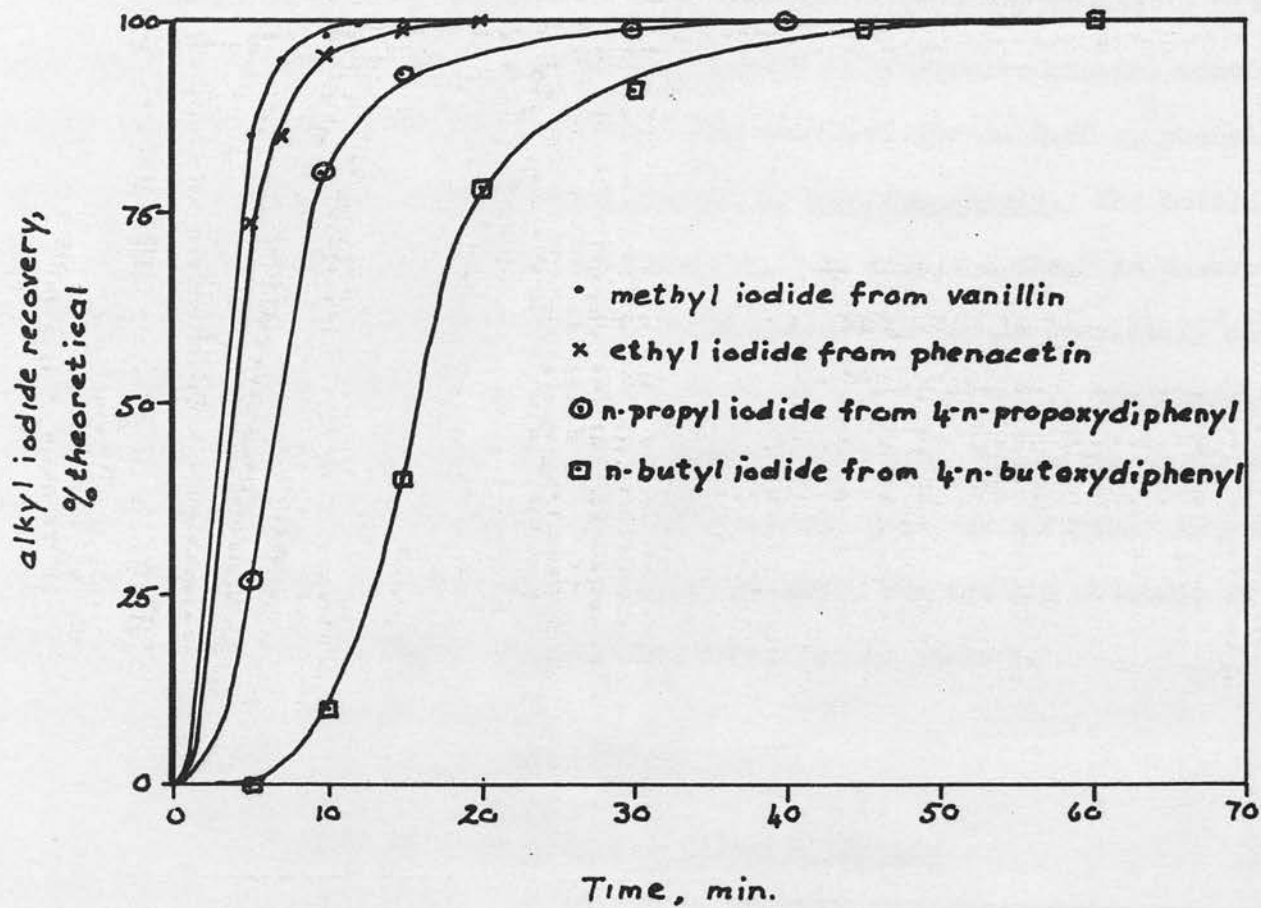


Fig. 3. Rates of release of alkyl iodides from reaction mixture with a nitrogen flow-rate of 6-8 ml./min.

quantitative yields of alkyl iodides from volatile liquids without the necessity of double distillation or any apparatus modification. There is no reason that the technique should not apply when the conventional iodometric procedure is used.

The sample is weighed in a long-handled micro weighing-bottle fitted with a leak-proof ground-glass stopper. The bottle is transferred to the reaction flask charged with a mixture of 6 ml. hydroiodic acid and approx. 0.25 g. phenol, conditioned as previously described, and allowed to cool completely. The bottle must submerge completely in the reaction mixture. The reaction flask is shaken to loosen the weighing-bottle stopper and to allow the sample to mix completely with the reaction mixture. Using a nitrogen flow-rate of 2 - 4 ml./min., the flask is heated gently so that ebullition commences after 8 - 10 min. The nitrogen flow-rate is then increased to 6 - 8 ml./min. and refluxing continued for a further 30 min. This procedure applies to methoxyl and ethoxyl groups. The results obtained on a variety of liquids of differing volatilities are given in Table 3.

TABLE 3

Alkoxy Determinations on Volatile Liquids

Compound	Boiling point, °C.	Weight taken, mg.	% alkoxy	
			found	theory
Methanol	65	(0.68	96.1	96.9
		(0.76	95.5	
1:1-dimethoxyethane	64.5	(0.78	69.5	71.1
		(0.92	70.9	
1:2-dimethoxyethane	86	(0.88	69.6	71.1
		(0.92	72.0	
Anisole	154	(2.34	28.5	28.7
		(5.14	28.8	
Ethyl orthoformate	146	(0.98	90.8	91.2
		(0.76	91.7	
Ethanol	78	(0.68	98.1	97.8
		(0.81	96.6	

The analysis of anisole has caused much difficulty in the past,<sup>5,15</sup> but, using the above procedure, reproducible results were easily obtained with this compound, (Table 3). It was shown that no detectable traces of unreacted anisole were volatilised, together with the methyl iodide, unless the nitrogen flow-rate was increased to more than 15 ml./min. The reason given<sup>15</sup> that volatilisation of the anisole from the reaction flask, under a slow flow-rate of carbon dioxide, was causing low analytical results appears, therefore, to be unfounded.

The Effect of the Presence of Sulphur in the Reaction Flask. The presence of sulphur has long been known to complicate alkoxy analyses, causing low results. Sulphur present in organic functional groups is reduced to hydrogen sulphide by reflux with hydriodic acid; inorganic sulphate reacts similarly. Usually, only one sulphur atom is present, but the ratio of sulphur atoms to alkoxy groups in compounds can exceed 1 : 1. It is of importance that the analysis of compounds mixed with relatively large amounts of inorganic sulphate has caused particular difficulty.<sup>48,49</sup>

Interaction between hydrogen sulphide and alkyl iodides, resulting in mercaptan formation is considered to cause the low results. Bethge and Carlson<sup>27</sup> have suggested that this reaction is favoured in alkaline solution. The infrared technique has shown that no reaction between hydrogen sulphide and alkyl iodides occurs in the vapour phase: alkoxy compounds containing sulphur, or to which had been added sodium sulphate, gave theoretical yields of alkyl iodide in presence of the evolved hydrogen sulphide, (see Table 4). The undesired interaction must therefore occur only in aqueous solution.

Mere absorption of hydrogen sulphide by wash liquids is therefore insufficient; quantitative removal of sulphide ions from solution is essential.

TABLE 4

Compound	Weight taken, mg.	Weight Na <sub>2</sub> SO <sub>4</sub> added, mg.	% alkoxy	
			found	theory
Dimethyl sulphate	3.86	--	49.0	49.2
4-aminoanisoie-3-sulphonic acid	7.76	--	15.3	15.3
O:O':O"-triethylphosphorothioate	1.31	--	67.8	68.2
6-bromo-2-ethoxy-N-toluene-p-sulphonyl-1-naphthylamine	6.72	--	10.6	10.7
Methyl-4:6-O-benzylidene- $\alpha$ -D-glucoside-2-toluene-p-sulphonate	7.90	--	7.06	7.12
Methyl-4:6-O-ethylidene- $\alpha$ -D-mannoside-3-nitrate-2-toluene-p-sulphonate	8.56	--	7.41	7.41
Vanillin	(2.90)	15	20.5	20.4
	(3.00)	30	20.4	
Phenacetin	(3.01)	15	25.2	25.1
	(3.06)	30	25.2	
n-propyl-3:5-dinitrobenzoate	(6.00)	30	23.1	25.2
	(5.79)	60	23.3	
n-butyl-3:5-dinitrobenzoate	(3.15)	15	27.5	27.5
	(3.03)	30	27.3	

Thus any wash liquid able to remove satisfactorily the large amounts of hydrogen sulphide liberated when excess inorganic sulphate is present will have a safety-factor when sulphur-containing organic compounds are analysed. The following investigation of the efficiency of wash liquids was made from this viewpoint.

The Efficiency of Aqueous Wash Liquids. Comparison of efficiencies were made using 4 ml. of solution in the B.S. (1954) design spiral scrubber, unless otherwise stated. A nitrogen flow-rate of 6 - 8 ml./min. was employed. Vanillin was the standard methoxyl compound used.

Results confirmed that aqueous sodium thiosulphate is unsatisfactory<sup>16</sup> because of reaction with methyl iodide.<sup>22,23</sup> Table 5 summarises the results obtained

TABLE 5

Efficiency of Some Scrubbing Solutions in Methoxyl  
Determinations in the Presence and Absence of Sulphur

Range of weight of Vanillin = 2.92 - 3.39 mg.; methoxyl present approx. 0.2 mEquiv.

Composition of scrubbing liquid (Vol. used = 4 ml.)	Weight $\text{Na}_2\text{SO}_4$ added, mg.	∴ sulphur present, mEquiv.	Range of methoxyl recovery, %
5% aq. sodium bicarbonate	0	0.0	99.4 - 100.4
	3	0.2	95.1 - 95.3
	10	0.7	92.5 - 92.7
	27	1.9	90.0 - 90.4
25% aq. sodium acetate	0	0.0	100.0 - 100.5
	4	0.3	98.1 - 98.5
	30	2.1	91.1 - 91.2
10% aq. sodium antimonyl tartrate	0	0.0	99.5 - 100.2
	3	0.2	99.6 - 100.0
	10	0.7	95.1 - 95.3
	15	1.0	94.1 - 94.2
5% aq. sodium thiosulphate + 5% aq. cadmium sulphate (1 + 1 V/V)	0	0.0	100.0 - 100.5
	3	0.2	100.0 - 100.1
	10	0.7	99.1 - 99.5
	18	1.3	97.7 - 98.0
5% aq. cadmium sulphate	0	0.0	} 99.8 - 100.6
	3	0.2	
	10	0.7	
	15	1.0	} 99.0 - 99.2
	32	2.2	
Water	2 ml.	0	99.5 - 99.7
	4 ml.	0	98.8 - 99.2
	2 ml.	4	97.5 - 97.9
	4 ml.	4	96.8 - 97.1
Water saturated with $\text{H}_2\text{S}$	2 ml.	0	95.2
	3 ml.	0	94.0
	4 ml.	0	91.3
	5 ml.	0	90.7

on the most generally advocated wash liquids. For each solution tested, several determinations were made under the conditions shown; the range of recoveries of methyl iodide is quoted, since averaged results at the 100% level can be misleading.

In the absence of sulphur all the wash solutions, except sodium thio-sulphate and cold water, gave satisfactory results. Cold water gave slightly low results; this is in agreement with Heron et al.<sup>16</sup> who reported 94 - 98% recovery. These negative errors are undoubtedly due to the solubility of methyl iodide in water; the effect can be minimised by maintaining the water at 42°C, (the boiling-point of methyl iodide), but this adds a complicating factor to the scrubber design. Although heated wash liquids have been recommended,<sup>1,50,51</sup> Colson has pointed out<sup>15</sup> that the increased possibility of hydrolysis of methyl iodide may lead to low results. As can be seen in Table 5, the negative error was dependent on the volume of water used, and large errors were introduced when sulphur was present. This may be compared with the results obtained using water saturated with hydrogen sulphide as a wash liquid. These results confirm that reaction between methyl iodide and hydrogen sulphide occurs in aqueous solution.

In the presence of 3 mg. added sodium sulphate, (equivalent to one sulphur atom per methoxyl group for 3 mg samples of vanillin), only sodium acetate and sodium bicarbonate of the solutions tested were unsatisfactory. This is in agreement with the statement of Bethge and Carlson that mercaptan formation is favoured in alkaline solution.<sup>27</sup>

In the presence of larger amounts of sulphur, both sodium antimonyl tartrate and sodium thiosulphate/cadmium sulphate mixture began to give low results. This finding explains the differing opinions expressed regarding their efficiencies.<sup>12,27,4,16,22</sup> In agreement with earlier investigators<sup>14,49</sup> cadmium sulphate gave good results; it was the only completely satisfactory wash liquid in the presence or absence of sulphur. The formation of heavy cadmium sulphide precipitates did not influence its efficiency, as had been suggested.<sup>52</sup> Consequently, a 5% aqueous cadmium sulphate solution is

recommended as the most satisfactory wash liquid to be used for routine analysis.

With high concentrations of hydrogen sulphide, the decreased efficiency of the sodium antimonyl tartrate wash liquid may be attributed to solubilisation of the original antimony sulphide precipitate as a result of complex thio-anion formation, and subsequent interaction between the thio-anion and methyl iodide. For cadmium sulphate, the concentration of hydrogen sulphide is not so critical, cadmium sulphide being unable to form complex sulphides. In solutions containing cadmium sulphate and sodium thiosulphate, complexing of thiosulphate ions by cadmium undoubtedly occurs. The decreased efficiency of this wash liquid at high sulphur concentrations is most probably due to removal from solution of cadmium ions as cadmium sulphide, thus liberating some of the previously complexed thiosulphate, which can then react with the alkyl iodide. The presence of thiosulphate in the wash liquid therefore appears to have no beneficial effect, and only serves to decrease its efficiency at high sulphur concentrations.

Many other aqueous wash liquids have been proposed, but not generally accepted. The efficiency of these were therefore not investigated.

The B.S. design spiral scrubber gives adequate scrubbing efficiency under the experimental conditions described, but not at greatly increased flow-rates. Using aqueous cadmium sulphate in two spiral scrubbers joined in series, no detectable leakage of hydrogen sulphide to the second scrubber occurred at flow-rates of up to 10 ml./min. Slight leakage occurred at 15 - 20 ml./min. This supports the earlier warning of Heron et al.<sup>16</sup> regarding scrubber efficiency and flow-rates of carrier gas used.

The Use of Solid Scrubbers. Having established that reaction between hydrogen sulphide and alkyl iodides occurs only in aqueous solution, it appeared that the use

of a suitable solid scrubber would eliminate several possible sources of error. The use of solid scrubbers was apparently first suggested by Fierz-David et al.,<sup>31</sup> but their use in alkoxy determination has attracted little attention until very recently.<sup>32,33,33</sup>

Experiments have shown soda asbestos (M.A.R.) to be a very efficient solid scrubber. It quantitatively absorbs hydrogen iodide, iodine, hydrogen sulphide and carbon dioxide; even when quantities of these vapours have been absorbed there is no retention of alkyl iodides. When 40 mg. sodium sulphate was refluxed with hydriodic acid for 3 hr., using a flow-rate of 40 ml./min., no hydrogen sulphide passed the scrubber. Table 6 shows the high efficiency of a soda asbestos solid scrubber under testing conditions. A nitrogen flow-rate of 6 - 8 ml./min.

TABLE 6

Efficiency of a Soda Asbestos Solid Scrubber in Alkoxy Determinations

Compound	Weight taken, mg.	Weight Na <sub>2</sub> SO <sub>4</sub> added, mg.	% alkoxy	
			found	theory
Vanillin	2.78	0	20.4	
	3.03	10	20.5	20.4
	3.00	30	20.4	
	2.75	60	20.2	
Phenacetin	3.21	0	25.0	
	5.42	30	25.0	25.1
	3.01	60	25.1	
n-propyl-3:5-dinitrobenzoate	5.82	0	23.5	
	5.79	30	23.2	23.2
	6.02	60	23.5	
n-butyl-3:5-dinitrobenzoate	3.15	0	27.4	
	3.03	40	27.2	27.3

was employed. The soda asbestos packing was renewed for each determination, and a little anhydrone was mixed with the packing to ensure removal of any water vapour.

Experimentally, the use of a solid scrubber simplifies the apparatus and procedure. Flow-rates become non-critical.<sup>32</sup> The use of nitrogen as carrier gas is essential. The spiral liquid scrubber is replaced by a straight connecting tube with a packing of soda asbestos about 2 in. long, which is renewed for each analysis.

Conclusions. It is considered that the foregoing survey has helped to clarify the rather confused situation in the literature on the determination of alkoxy groups. Definite conclusions regarding the best combination of experimental conditions for routine analysis can be made.

- a) Constant-boiling hydriodic acid should be used for all determinations. The colour of the acid is non-critical, unless very dark, when its disuse is merited.
- b) Up to 8 successive determinations may safely be carried out on the same sample of acid, provided conditioning of the acid is performed between each determination.
- c) Extended reaction periods are not desirable. For methoxyl and ethoxyl determinations, using a flow-rate of 6 - 8 ml./min., 30 min. reflux is sufficient. For propoxyl and butoxyl determinations, reflux periods of 60 min. and 75 min., respectively, are amply sufficient.
- d) Cold condenser water should be used for all determinations.
- e) For routine analysis, aqueous cadmium sulphate is a most efficient wash liquid, whether in the absence or in the presence of any amounts of sulphur.
- f) The use of soda asbestos as a solid scrubber is strongly advocated. Apparatus and experimental procedure are simplified, and flow-rates become non-critical as regards scrubbing, but will be determined by the efficiency of absorption of the

alkyl iodides.

The Simultaneous Determination of Methyl

and Ethyl Groups by Infrared Spectroscopy

It is considered that the reaction conditions described above are totally applicable to alkoxy determinations in which the standard gravimetric or iodometric finish is employed.

only gives results comparable in accuracy and reproducibility with those obtainable by the more conventional methods (see Tables 1, 2 and 3), but also distinguishes in the same analysis between different alkyl groups. Of unknown compounds, this selective information cannot be obtained directly if the conventional iodometric or gravimetric finishes are employed.

The majority of simultaneous methoxy/ethoxy determinations have required this cumbersome modification or application to the standard iodometric techniques. Techniques based on Martin and Verzeletti's<sup>14</sup> use of gas chromatography later introduced<sup>15,16</sup> have offered possibilities for future development, but more recent publications have merely reverted to modifying the Willstätter and Hildreth techniques<sup>17</sup> using alcoholic trimethylamine as absorbent, or to describing modifications<sup>18,19</sup> of Friedrich's oxidation method.<sup>21</sup>

The quantitative infrared technique can be extended, without modification or loss in accuracy, to the simultaneous determination of methoxy and ethoxy groups. Results, correct to within 1% for both groups, can be obtained on a single sample weight. The presence of sulfur in any form causes no interference.

Procedure. The procedure used was exactly as described for the independent determination of methoxy and ethoxy groups - 10 mg. reflex with a nitrogen flow rate of 3 - 5 ml./min., the volatile products being trapped in liquid nitrogen.

Fig. 4 diagrammatically represents the spectra given by methyl iodide, ethyl iodide, and by a mixture of the two in the 1500 - 800  $cm^{-1}$  region. In the

2. The Simultaneous Determination of Methoxyl and Ethoxyl Groups by Infrared Spectroscopy.

The spectroscopic method of determining liberated alkyl iodides not only gives results comparable in accuracy and reproducibility with those obtainable by the more conventional methods (see Tables 1,2 and 3), but also distinguishes in the same analysis between different alkoxy groups. On unknown compounds, this selective information cannot be obtained directly if the conventional iodometric or gravimetric finishes are employed.

The majority of simultaneous methoxyl/ethoxyl determinations have required time-consuming modification or extension to the standard Zeisel technique. Techniques based on Martin and Vertalier's<sup>54</sup> use of gas chromatography later introduced<sup>55,56</sup> have offered possibilities for future development, but more recent publications have merely reverted to modifying the Willstätter and Utzinger technique<sup>37</sup> using alcoholic trimethylamine as absorbent, or to describing modifications<sup>32,42</sup> of Friedrich's combustion method.<sup>21</sup>

The quantitative infrared technique can be extended, without modification or loss in accuracy, to the simultaneous determination of methoxyl and ethoxyl groups. Results, correct to within  $\pm 1\%$  for both groups, can be obtained on a single sample weight. The presence of sulphur in any form causes no interference.

Procedure. The procedure used was exactly as described for the independent determination of methoxyl and ethoxyl groups -- 30 min. reflux with a nitrogen flow-rate of 6 - 8 ml./min., the volatile products being trapped in liquid nitrogen.

Fig. 4 diagrammatically represents the spectra given by methyl iodide, ethyl iodide, and by a mixture of the two in the 1500 - 800  $\text{cm.}^{-1}$  region. In the

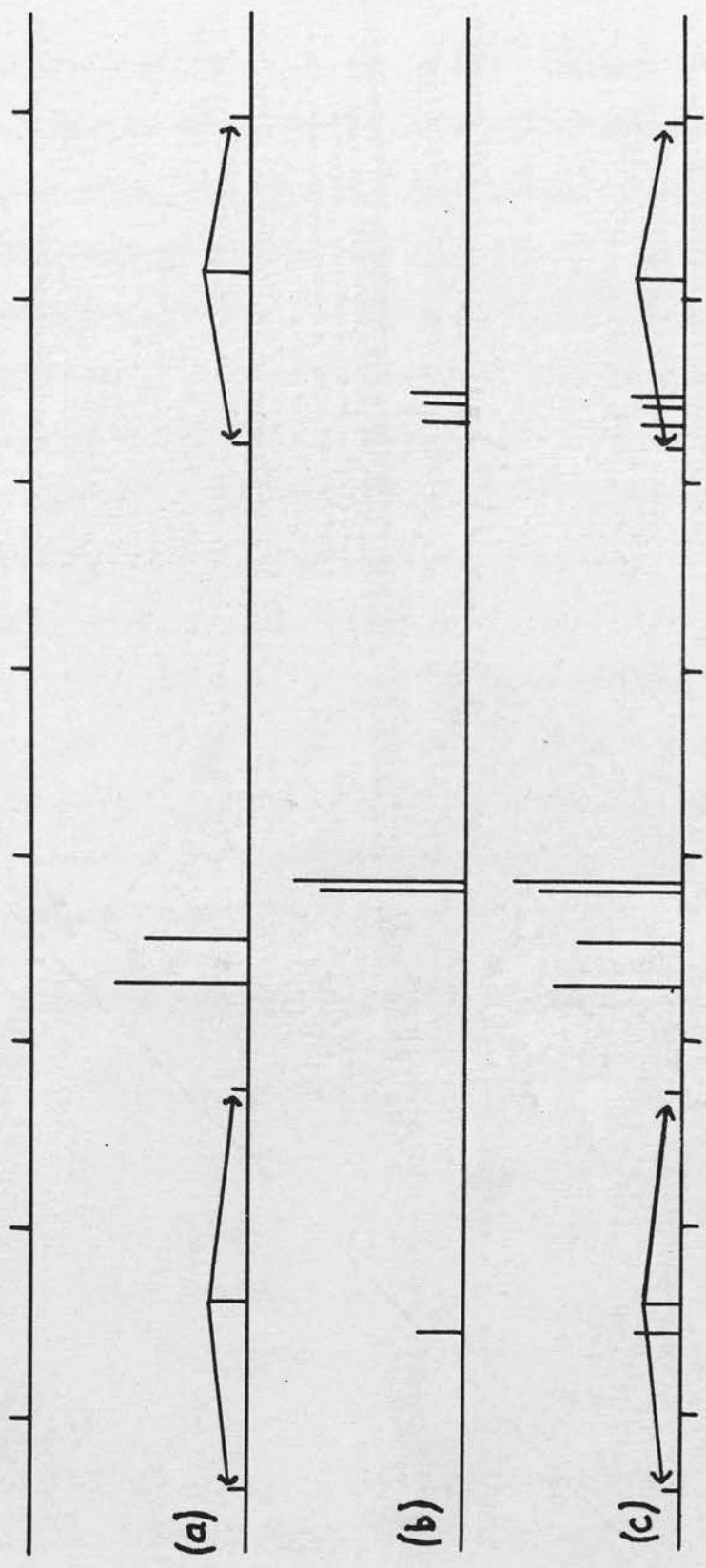


Fig. 4. Infrared spectra from  $1500-800\text{ cm}^{-1}$  of methyl iodide (a) and ethyl iodide (b) and composite spectrum (c) of a mixture of the two iodides.

composite spectrum (Fig. 4c), very slight overlapping of major peaks occurs; the 1242  $\text{cm.}^{-1}$  peak of methyl iodide fractionally increasing the height of the 1216  $\text{cm.}^{-1}$  ethyl iodide peak. The 1264  $\text{cm.}^{-1}$  methyl iodide peak is not masked and so calibrations based on it give correct methoxyl values. Calibration based on the 1216  $\text{cm.}^{-1}$  ethyl iodide peak, however, led to high ethoxyl values in this circumstance. The more minor peaks given by ethyl iodide at 1453  $\text{cm.}^{-1}$  and 955  $\text{cm.}^{-1}$  are also subject to overlapping by minor methyl iodide peaks, and so could not be used. Fortunately, this positive ethoxyl error was found to be a linear function of the weight of methyl iodide present and a correction factor, applicable to a particular set of standard spectrometer conditions, was calculable. When  $(0.019) \times$  (weight of methyl iodide found) was subtracted from the actual weight of ethyl iodide found, the results shown in Table 7 were obtained for methoxy-ethoxy compounds or for synthetic mixtures ranging in composition from methoxyl/ethoxyl = 5:1 to 1:5.

TABLE 7

Results for Simultaneous Methoxyl/Ethoxyl Determinations

Compound or mixture	Weight taken, mg.	Weight alkyl iodide found,		Corrected* weight ethyl iodide found, mg.	% methoxyl		% ethoxyl	
		MeI mg.	EtI mg.		found	theory	found	theory
Vanillin )	7.41	6.94			20.4	20.4		
Phenacetin )	5.29		5.00	2.86			25.2	25.1
Vanillin )	10.24	9.52			20.3	20.4		
Phenacetin )	3.02		2.82	2.63			25.3	25.1
Vanillin )	2.05	1.90			20.5	20.4		
Phenacetin )	4.28		5.75	5.71			25.1	25.1
Anisic acid )	9.45	8.72			20.2	20.4		
Compound X† )	7.20		5.15	2.98			12.0	12.0
Compound Y†	2.60	6.26	2.40	2.28	52.7	52.3	25.8	25.3
Compound Z†	1.42	0.98	3.22	3.20	15.1	15.0	65.1	65.5

\* Corrected weight Ethyl iodide = (weight EtI found) - (0.019)(weight MeI found)

† Compound X: 4-chloro-2-ethoxy-p-tosyl-1-naphthylamine

Compound Y: 1:1:3-trimethoxy-3-ethoxypropane

Compound Z: 1:1:3-triethoxy-3-methoxypropane

At low ethoxyl contents, the  $1216 \text{ cm.}^{-1}$  ethyl iodide absorption occurred as a shoulder on the  $1242 \text{ cm.}^{-1}$  methyl iodide peak, and determinations became inaccurate. At methoxyl/ethoxyl ratios greater than 4:1 there was no measurable ethyl iodide peak height and the method failed. Although such combinations must be very rare in actual chemical compounds, they could readily be met with in determinations on mixtures of methoxyl and ethoxyl compounds. Such mixtures can be analysed by the infrared method by the use of constant-boiling hydrobromic acid in place of the customary hydriodic acid.

Methoxyl/Ethoxyl Determinations using Hydrobromic Acid. Constant-boiling hydrobromic acid (specific gravity 1.47) is effective in cleaving alkoxy groups; it produces alkyl bromides quantitatively from esters and ethers almost as rapidly (15 - 20 min. for methyl and ethyl) as hydriodic acid forms the corresponding iodides. Alkyl bromides are as conveniently estimated as alkyl iodides by the infrared method if the required calibration curves are constructed. That for ethyl bromide (b.p.  $38^{\circ}\text{C.}$ ) may be constructed by direct weighing as previously described. However, the calibration curve for methyl bromide (b.p.  $5.6^{\circ}\text{C.}$ ) must be constructed by means of the manometric technique previously described by Anderson.<sup>45</sup> This involves the use of the ideal gas law to estimate weights from accurately known pressures of gas introduced into the gas-cells. The  $1520 \text{ cm.}^{-1}$  absorption of methyl bromide is so widely separated from the  $1250 \text{ cm.}^{-1}$  peak of ethyl bromide that calibrations based on each of these are valid for the analysis of all possible methoxyl/ethoxyl percentage compositions. The only slight disadvantage in the use of the bromides is the small decrease in sensitivity, requiring that larger sample weights be taken, as compared with those required when hydriodic acid is used.

Table 8 shows representative results obtained for simultaneous

TABLE 8

Simultaneous Methoxyl/Ethoxyl Determinations using Hydrobromic Acid

Compound or mixture	Weight taken, mg.	Weight alkyl iodide found,		% methoxyl		% ethoxyl	
		MeBr mg.	EtEr mg.	found	theory	found	theory
Vanillin ) Phenacetin)	3.17 3.24	2.94	2.79	20.5	20.4	24.9	25.1
Vanillin ) Phenacetin)	1.76 4.17	1.65	3.65	20.2	20.4	25.3	25.1
Vanillin ) Phenacetin)	1.15 4.42	1.06	3.86	20.2	20.4	25.2	25.1
Compound Y*	3.02	7.14	2.68	51.7	52.3	25.6	25.3

\* Compound Y: 1:1:3-trimethoxy-5-ethoxypropane

methoxyl/ethoxyl determinations using hydrobromic acid. The results are equal in accuracy to those shown in Table 7, and were obtained without the necessity of using a correction factor.

Conclusions. The methods described above permit satisfactory simultaneous determinations of methoxyl and ethoxyl groups on the micro scale. The accuracy obtainable, small sample weight required, short reaction time, elimination of conventional scrubbers, and absence of interference from sulphur combine to make the infrared spectroscopic method simpler, quicker, and superior to any method previously described for the simultaneous determination of alkoxy groups.

3. Anomalous Reactions in the Alkoxy Determination.

This section may conveniently be divided into two parts:

- a) Anomalous results arising from cleavage of certain alkimide groups under Zeisel alkoxy reaction conditions;
- b) An explanation of the causes of anomalous results given by sugars, polysaccharides and polyhydric alcohols.

a) Anomalous Results arising from Cleavage of Certain Alkimide Groups. The determination of alkimide groups<sup>31,57,58</sup> requires drastic treatment of the compound in question with hydriodic acid. The differences in ease of cleavage of alkoxy and alkimide groups is generally so great that both may be successively determined on a single sample containing both functional groups.<sup>58</sup> By carrying out the customary alkoxy determination and then distilling the hydriodic acid into a second reaction flask joined in series to the first, and pyrolysing the remaining ~~the remaining~~ quaternary ammonium salt at about 350°C., both the alkoxy and alkimide content of a single sample can be determined, by successive estimations of the alkyl iodide liberated.

Steyermark,<sup>46</sup> however, has called attention to the fact that occasionally an  $\text{NCH}_3$  or  $\text{NC}_2\text{H}_5$  group might be mistaken for an  $\text{OCH}_3$  or  $\text{OC}_2\text{H}_5$  group. Recently, he has encountered several compounds whose structures were definitely known and which contained only alkimide groups, but which all yielded methyl or ethyl iodides in boiling hydriodic acid.

In performing alkoxy determinations by the infrared method on a series of Ehrlich-Sachs esters, (prepared by condensation of NN-dialkyl-p-nitrosoanilines

with cyanoacetic esters, and kindly provided by Prof. F. Bell), the same effect has been observed. These compounds are of general formula  $R_2N-\text{C}_6\text{H}_4-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{R}'$ , and it was found that when  $R = \text{CH}_3$  a slow liberation of methyl iodide from the alkimide group proceeded over a period of several hours. When  $R = \text{C}_2\text{H}_5$  the liberation of ethyl iodide was not so great and in some cases did not appear to occur. The di-n-propylamino group was not labile under the reaction conditions. In the cases when R and R' were different, simultaneous determinations of the two liberated iodides were possible. When the two groups were the same, high results for the alkoxy content were obtained. The results are summarised in Table 9.







TABLE 9

Anomalous Alkoxy Results obtained from Ehrlich-Sachs Esters

Compound	Weight taken, mg.	Reaction time, hr.	% methoxyl		% ethoxyl	
			found	theory	found	theory
$\text{Me}_2\text{N}-\text{C}_6\text{H}_4-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{Me}$	4.00	1	14.1	15.4	0.0	0.0
	5.96	2	14.7	15.4	0.0	0.0
$\text{Me}_2\text{N}-\text{C}_6\text{H}_4-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{Et}$	6.02	1	2.7	0.0	18.5	18.4
	5.08	2	4.0	0.0	18.2	18.4
$\text{Me}_2\text{N}-\text{C}_6\text{H}_3(\text{Me})-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{Me}$	5.97	1	13.4	12.7	0.0	0.0
	4.06	2	14.1	12.7	0.0	0.0
$\text{Me}_2\text{N}-\text{C}_6\text{H}_3(\text{Me})-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{Et}$	2.62	1	3.0	0.0	17.4	17.4
	2.51	2	5.8	0.0	17.5	17.4
$\text{Et}_2\text{N}-\text{C}_6\text{H}_3(\text{Me})-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{Me}$	6.99	1	11.4	11.4	1.6	0.0
	6.97	2	11.4	11.4	3.0	0.0
$\text{Et}_2\text{N}-\text{C}_6\text{H}_4-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{Et}$	6.42	1	0.0	0.0	15.8	15.7
	5.56	2	0.0	0.0	15.6	15.7
$\text{MeNH}-\text{C}_6\text{H}_4-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{Me}$	4.65	1	20.5	14.5	0.0	0.0
	4.61	2	24.8	14.5	0.0	0.0
$\text{MeNH}-\text{C}_6\text{H}_4-\text{N}:\text{C}(\text{CN})\cdot\text{CO}_2\text{Et}$	4.27	1	2.8	0.0	19.5	19.5
	4.39	2	5.0	0.0	19.4	19.5

When the parent p-nitrosoanilines and other Ehrlich-Sachs products not containing alkoxy groups were treated with hydriodic acid, all were found to slowly release methyl iodide from the  $N(CH_3)_2$  or  $NHCH_3$  group for several hours, as shown in Table 10.

TABLE 10

Compound	Weight taken, mg.	Reaction time, hr.	% methoxyl	
			found	theory
$Me_2N$ -  - $N:O$	8.75	1	2.1	0.0
	5.50	2	3.6	0.0
	9.25	3	4.5	0.0
$MeNH$ -  - $N:O$	7.85	1	5.3	0.0
	7.85	2	6.3	0.0
$Me_2N$ -  - $N:C(CN).Ph$	11.20	2	1.8	0.0
$Me_2N$ -  - $N:C(CN)_2$	5.31	2	2.5	0.0
$Me_2N$ -  - $N:C(CN).C(NH_2).C(CN)_2$	10.98	2	2.0	0.0
$Me_2N$ -  - $N:C(CN).Ph$	19.02	2	2.0	0.0

Care must always be exercised, therefore, in interpreting alkoxy results from compounds known also to contain alkimide groups. There is no reason to suppose that the above series are by any means unique; when successive determinations on unknown compounds are being performed using the same sample of hydriodic acid, the possibility of slow release of alkyl iodides over a long period must always be considered.

b) The Causes of Anomalous Alkoxyyl Results given by Sugars and Polysaccharides.

Zeisel determinations on unmethylated sugars and polysaccharides have been reported<sup>59,60</sup> to give small apparent alkoxyyl values. This implied that all carbohydrate materials would give slightly high analytical results, and has made particularly difficult the interpretation of analyses of polysaccharide fractions having a small but real methoxyyl content. The identity of the volatile products from carbohydrate materials, and the sources of error contributing to the anomalous results, have hitherto not been clearly established. For simple sugars, Gran<sup>60</sup> has suggested that the formation of volatile hexyl iodides is responsible, although he did not isolate or identify such products. Clearly further investigation into this subject was desirable.

30 - 60 mg. samples of the compounds listed in Table 11 were refluxed for 1 hr. with constant-boiling, pre-conditioned hydriodic acid. The mixture of volatile products was collected, after passage through anhydrone, in a trap immersed in liquid nitrogen. The components of each mixture were subsequently identified and quantitatively estimated by vapour-phase infrared spectroscopy, and are listed in Table 11. To establish the effect of varying the reaction time and sample weight, experiments were performed on glucose (M.A.R.) as a standard compound, and the results are shown in Table 12.

When a carbohydrate material is suspected of having a low methoxyyl content, large sample weights must be employed if the methyl iodide released is to be determined accurately. There is also a tendency for reflux periods longer than normal to be used.<sup>60</sup> Table 12 shows that, up to a certain ratio, (ca. 100 mg. sample per 6 ml. hydriodic acid), the volatile products from sugars are independent of the sample weight taken. For larger samples, different decomposition mechanisms are

TABLE 11

Volatile Reaction Products released from Carbohydrates and Related Substances on refluxing with Hydriodic Acid

Compound reacted*	Yield <sup>†</sup> of volatile products <sup>//</sup>					
	n-heptane	n-hexane	n-pentane	n-butane	2:5-di-methylfuran	acetone
Glucoheptose	tr	--	--	--	--	--
2-deoxyglucose	--	tr	--	--	--	--
Glucose and Hexoses	--	tr	--	--	2%	--
Fructose and Sorbose	--	1%	--	--	2%	--
Rhamnose and Fucose	--	1%	--	--	2%	--
Glucosamine hydrochloride	--	tr	--	--	tr	tr
Sucrose	--	tr	--	--	2%	1%
Glucurone <sup>a</sup>	--	--	tr	--	--	--
Xylose and Pentoses	--	--	tr	--	--	--
5-ketogluconolactone <sup>b</sup>	--	--	tr	--	--	--
Galactonolactone <sup>c</sup>	--	--	tr	--	--	tr
Erythrose	--	--	--	tr	--	1%
Glyceraldehyde	--	--	--	--	--	1%
Oat starch	--	tr	--	--	1%	--
Waxy maize starch	--	tr	--	--	3%	tr
Glycogen (ex mussel)	--	tr	--	--	3.5%	tr
Inulin	--	tr	--	--	4.5%	tr
Agar	--	tr	--	--	2%	tr
Cellulose	--	tr	--	--	2%	tr
Araboxylan	--	--	tr	--	--	--

\* 30 - 60 mg. in 6 ml. hydriodic acid under reflux for 1 hr.

† Expressed as % of weight of sample taken; tr denotes < 0.02%.

// In addition to the products shown, all compounds gave a trace of carbon dioxide, except for a, b and c, which gave approx. 0.75 mole CO<sub>2</sub> per mole of compound.

TABLE 12

Variation of Volatile Reaction Products with Weight  
of Sample and Reaction Time for Glucose/Hydriodic Acid

Weight of glucose reacted,* mg.	Reaction time, hr.	Yield <sup>†</sup> of volatile products
20 - 100	1	CO <sub>2</sub> (tr) + n-hexane (tr) + 2:5-dimethylfuran (2%)
20 - 100	4	CO <sub>2</sub> (tr) + n-hexane (tr) + 2:5-dimethylfuran (4%)
250	1	CO <sub>2</sub> (tr)
500	1	CO <sub>2</sub> (tr) + methyl iodide (0.12%)
500	3	CO <sub>2</sub> (tr) + methyl iodide (0.40%)

\* Reacted with 6 ml. hydriodic acid under reflux.

† Yields expressed as % of weight of sample taken; tr denotes < 0.02%.

clearly involved, and Table 12 shows that, when exceptionally large weights of sugars are reacted (ca. 500 mg. per 6 ml. hydriodic acid), a small amount of methyl iodide is released, equivalent to 0.03% and 0.13% methoxyl after 1 and 3 hr. respectively. If Gran<sup>60</sup> used such large sample weights, (he does not state the weights used), this could explain his values of 0.1 - 0.4% apparent methoxyl for different sugars after 4 hr. reaction time.

However, with smaller sample weights, anomalous results of 0.01% to 0.05% methoxyl have been reported.<sup>59</sup> Alternative sources of error were therefore investigated. A brief survey of the reaction products in Table 11 revealed that all the sugars and polysaccharides produced trace amounts of an alkane, and variable quantities of acetone and/or 2:5-dimethylfuran. In so doing, large quantities of iodine were liberated in the reaction mixture. No alkyl iodides, however, were

liberated. These were only formed from the corresponding polyhydric alcohols, as shown in Table 13. This, therefore, refutes the suggestion made by Gran,<sup>60</sup> and proves

TABLE 13

Volatile Reaction Products from Polyhydric Alcohols/Hydriodic Acid

Compound reacted *	Yield <sup>†</sup> of volatile products
Sorbitol (10 - 30 mg.)	CO <sub>2</sub> (tr) + n-hexane (tr) + 2-iodohexane (~30%)
Mannitol (10 - 30 mg.)	CO <sub>2</sub> (tr) + n-hexane (tr) + 2-iodohexane (~30%)
Ribitol (10 mg.)	CO <sub>2</sub> (tr) + n-pentane (tr) + 2-iodopentane (~60%)
Erythritol (5 mg.)	CO <sub>2</sub> (tr) + 2-iodobutane (~80%)
Glycerol (5 mg.)	iso-propyl iodide (100%) (See ref. 26)
Ethylene glycol (5 mg.)	ethylene + ethyl iodide) (100%) (See ref. 61)

\* Reacted with 6 ml. hydriodic acid under reflux for 1 hr.

† Yields of alkyl iodides expressed as % of maximum possible alkyl release, formed by complete conversion of the polyhydric alcohol to the corresponding alkyl iodide.

that hydriodic acid is incapable of reducing sugars to their corresponding polyhydric alcohols. Alternative possible sources of error investigated were (i) volatilisation of the iodine produced in the reaction mixture, and (ii) the formation of alkanes, acetone, and 2:5-dimethylfuran.

(i) Volatilisation of Iodine. With 30 - 60 mg. samples of glucose, the amounts of iodine released were found to be insufficient to pass the condenser. With 250

and 500 mg. samples, however, a large sublimate of iodine formed on the condenser walls and some of the iodine was found to reach the cold trap. The efficiency of removal of such quantities of iodine by the recommended 10% aqueous sodium antimonyl tartrate solution<sup>12</sup> in the B.S. design of scrubber was therefore tested. When 100 mg. iodine was added to refluxing, preconditioned hydriodic acid, the amount of iodine passing the scrubber increased the reagent blank from 0.05 ml. 0.01N sodium thio-sulphate to 0.06 ml. (Cf. ref. 12). When 500 mg. glucose was refluxed, the apparent methoxyl content found iodometrically was equivalent to the amount of methyl iodide found by the infrared method in a duplicate run. The results are therefore in agreement with Belcher et al.<sup>12</sup> that iodine is not totally retained by the aqueous scrubber, but the amounts passing the scrubber are very small, even under testing conditions, and quite insufficient to account for the anomalous alkoxy values reported.

(ii) Result of formation of Alkanes, Acetone and 2:5-dimethylfuran. The alkanes liberated were not retained by the scrubbers normally employed. n-butane, n-pentane, n-hexane and n-heptane were found not to interfere with the iodometric determination, although a sluggish starch end-point was observed, caused perhaps by slight solvent-extraction of the iodine. It is doubtful that acetone would bypass an <sup>u</sup>aqueous scrubber, but it was found to cause negligible interference with the iodometric determination.

2:5-dimethylfuran bypasses aqueous and solid scrubbers, and the absorption of this compound in the oxidising solution (bromine/acetic acid/potassium acetate) permits a new explanation of the anomalous results to be given.

When 10, 20, 30, and 40 mg. 2:5-dimethylfuran was added to four 5 ml. portions of the oxidising solution, a reaction, clearly involving bromine, took place. A precipitate, found to be potassium bromide, was produced. When the determination was completed in the usual way, the thiosulphate titres indicated, when

carried out immediately, apparent additions of 0.9 mg. methyl iodide per 100 mg. 2:5-dimethylfuran. If the customary time of 10 min. was allowed to elapse before titration, the titres were equivalent to 1.8 mg. methyl iodide per 100 mg. 2:5-dimethylfuran, indicating 0.4% apparent methoxyl. Slow liberation of iodine continued for 5 hr., when the apparent methoxyl content reached 1.2%. Furan and 2-methylfuran reacted similarly, but liberated much smaller quantities of iodine than 2:5-dimethylfuran. The effect of 2:5-dimethylfuran was not associated with addition of excess formic acid to destroy bromine,<sup>62</sup> or excess sodium acetate and sulphuric acid,<sup>62</sup> and clearly contributes to the anomalous Zeisel reaction of sugars.

When furan is added to a cold solution of bromine in acetic acid containing potassium acetate, potassium bromide is precipitated, and 2:5-diacetoxy-2:5-dihydrofuran is produced in good yield.<sup>63</sup> This is readily hydrolysed to maledialdehyde in aqueous acid solution. Experiments showed that 2-methyl- and 2:5-dimethyl-furan react analogously to furan, although the respective products were too unstable to be isolated from the reaction mixture.<sup>64,65</sup> The following facts suggest that the unsaturated keto-compounds formed on hydrolysis are involved in the liberation of titratable iodine: a) iodine is released continuously for 4 - 5 hr., and b) the relative instabilities of the diacetoxy addition products increase in the order furan, 2-methylfuran, 2:5-dimethylfuran, which is the order of increasing yields of iodine by these substances.

Pathway A in Fig. 5 shows a possible reaction mechanism for the unexpected formation of 2:5 -dimethylfuran, VI, from hexoses, I. When 5-methylfurfural, VIII, was refluxed with hydriodic acid, extensive resinification occurred, and no 2:5-dimethylfuran was produced. Pathway B, therefore, does not account for the formation of 2:5-dimethylfuran. Pathway A explains all the experimental facts;

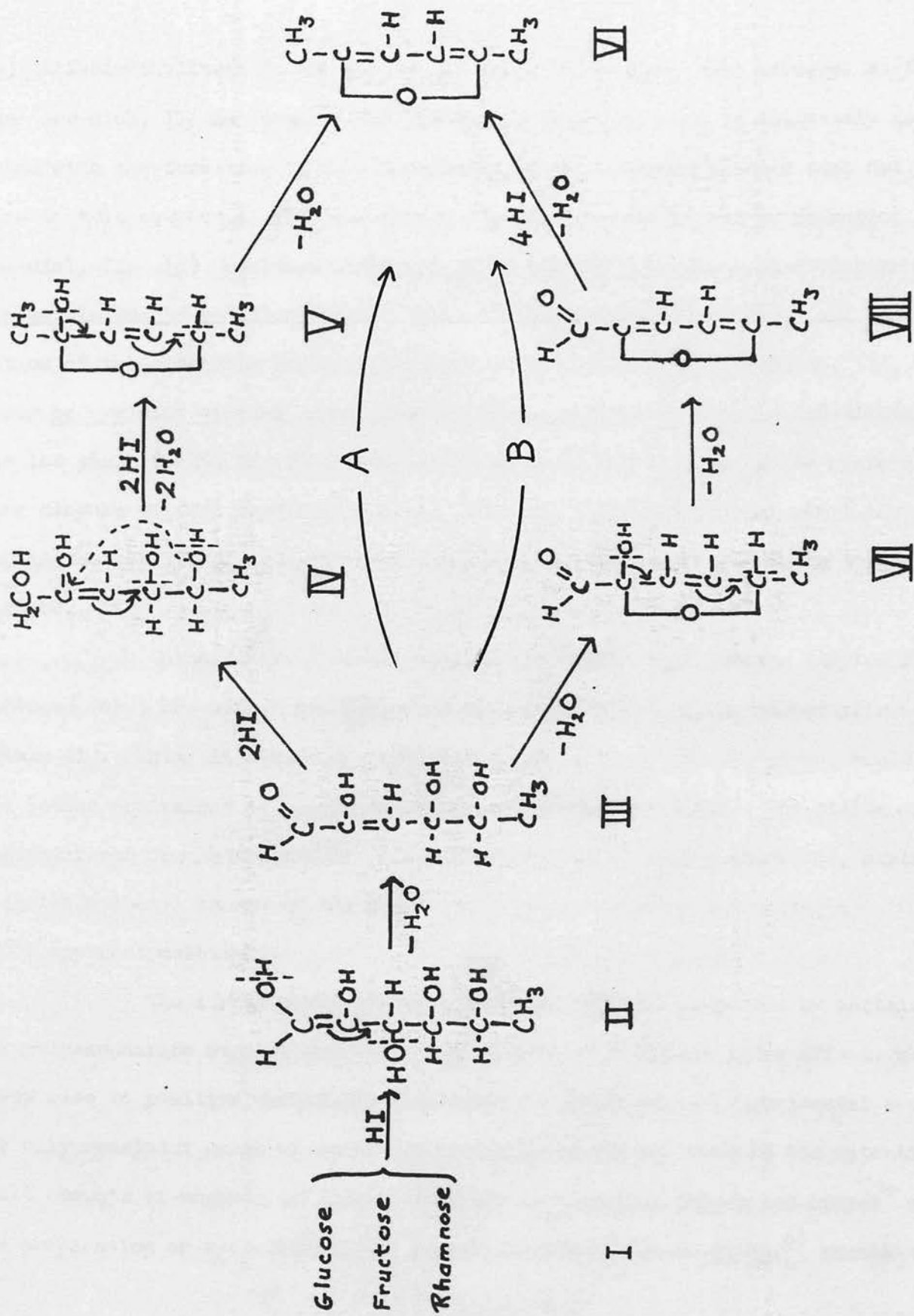


Fig.5. Possible mechanism for the formation of 2:5-dimethylfuran by the action of hydriodic acid on hexoses.

(a) 2:5-dimethylfuran is produced from both aldehydic and keto hexoses, as the same ene-diol, II, is formed; (b) an oxygen function on C<sub>2</sub> is intimately associated with the formation of 2:5-dimethylfuran, since 2-deoxyglucose does not give rise to this compound; (c) hexahydric alcohols are not formed by reduction of the ene-diol, II; (d) pentoses give rise to no 2:5-dimethylfuran, ring closure being impossible due to reduction of the terminal primary alcoholic group; and (e) reduction of the aldehydic group in the  $\alpha:\beta$ -unsaturated  $\alpha$ -hydroxyaldehyde, III, must occur before ring closure, since 5-methylfurfural gives rise to no 2:5-dimethylfuran. The low yield ( $\sim 2\%$ ) of 2:5-dimethylfuran obtained may well be due to preferential ring closure to form 5-methylfurfural, (that is, Pathway B is preferentially followed during the reaction), since a large degree of resinification occurs in the reaction mixture.

Quantitative infrared experiments showed that 100 mg. samples of hexoses refluxed for 1 hr. with 6 ml. hydriodic acid liberated 2 mg. 2:5-dimethylfuran, (Table 11). This, it can be calculated from the results already given, would liberate iodine equivalent to an apparent methoxyl content of 0.01%. The yields of 2:5-dimethylfuran from hexoses (2%) and polysaccharides (3 - 5%), therefore, explain positive methoxyl errors of the magnitude reported by Adams and Castagne<sup>59</sup> (0.01% - 0.05% apparent methoxyl).

The larger errors ( $>0.1\%$  apparent methoxyl) reported by certain authors for polysaccharide samples cannot be wholly attributed to the above effect, which gives rise to positive deviations almost within the limits of experimental error. The only remaining cause of such anomalous results may be found in the retention of small amounts of organic solvents, particularly alcohols, esters and ethers, used in the preparation or isolation of the polysaccharides. Jansen et al.<sup>66</sup> warned that

pectic materials were particularly liable to give this effect, and the warning has been repeated more recently<sup>67</sup> with regard to wood products. Experiments<sup>68</sup> have shown that organic solvents used to de-fat or dehydrate polysaccharide materials are retained up to temperatures at which the materials begin to decompose, despite oven and high-vacuum drying at temperatures much higher than the boiling points of the solvents involved (cf. ref. 66). Although pectic materials and plant gums gave the greatest retention, starches retained smaller, but easily measurable, quantities of solvents (cf. ref. 69). Errors greater than an apparent 0.1% methoxyl for polysaccharide materials may therefore most probably be attributed to this effect.

It is suggested that polysaccharide materials isolated with the aid of organic solvents, particularly alcohols, should be redissolved, dialysed, and freeze-dried, wherever possible, otherwise misleading results may be given in alkoxy analyses. When dialysing and freeze-drying are not possible, the use of methanol and methoxy compounds should be avoided; analysis by one of the valid methods<sup>58,70</sup> for methoxyl in the presence of other alkoxy groups can then be used.

#### Anomalous Alkoxy Results from Polyhydric Alcohols.

#### Evidence refuting von Rudloff's Proposal of the Formation of Vinyl Iodide.

It has long been known that glycerol and hexahydric alcohols, on treatment with hydriodic acid, liberate iso-propyl iodide and 2-iodohexane, respectively. Recently, however, von Rudloff<sup>71</sup> has proposed that the formation of vinyl iodide contributes to the anomalous alkoxy results given by polyhydric alcohols. On passing the volatile reaction products from ethylene glycol/hydriodic acid through a permanganate/periodate absorption solution, tests on the latter revealed the presence of formaldehyde. This, von Rudloff proposed, could only have come from vinyl iodide

with its  $\text{CH}_2\text{:CH-}$  grouping. Tests with higher polyhydric alcohols, however, gave only very dubious evidence of the production of vinyl iodide.

The infrared spectroscopic technique has shown that the production of vinyl iodide in hydriodic acid solution is impossible. Vinyl ester or ether linkages are readily cleaved by aqueous acid to produce acetaldehyde -- (this is the standard method for the estimation of vinyl groups). Hydriodic acid is incapable of converting acetaldehyde to vinyl iodide. Reaction of vinyl ethyl ether and vinyl propionate with hydriodic acid, in the usual manner for volatile liquids, revealed that no vinyl iodide or acetaldehyde were produced as volatile reaction products; presumably the latter, under the influence of acid, polymerises to paraldehyde which is involatile. When acetaldehyde was refluxed with hydriodic acid, none of the former was found to distil over from the reaction flask.

Table 13 shows that none of the most common polyhydric alcohols give rise to vinyl iodide as a volatile reaction product. von Rudloff's proposal is based on an erroneous assumption. Ethylene glycol has been known since Morgan's experiments<sup>72</sup> to give rise to ethyl iodide + ethylene (sum total = 100%) when treated with hydriodic acid. Ethylene, on absorption by a permanganate/periodate solution, readily produces formaldehyde, and clearly von Rudloff, by identifying only the final product, chose the wrong compound as the source of the anomaly. It is not surprising that polyhydric alcohols higher than ethylene glycol gave only very dubious evidence for the production of "vinyl iodide" since none of these produce any ethylene or unsaturated hydrocarbon on reaction with hydriodic acid (Table 13).

released is obtained, which can be assigned to a definite number of ester groups present in the molecule, if its molecular weight is known.

If the molecule contains ester and ether groups of the same alkyl

4. The Differentiation of Ester from Ether Groups in the Alkoxy Determination.

No method for the differentiation of ester from ether groups in the alkoxy determination is to be found in the literature. Such information would be advantageous when structural studies on unknown compounds are being made. With the infrared technique a simple modification enables this differentiation to be carried out.

It was found that constant-boiling hydrochloric acid quantitatively cleaved methyl and ethyl ester groups and formed the corresponding alkyl chlorides in 3 hours. Over a similar period the effect of the acid on normal ether linkages was negligible, only a trace of alkyl chloride being liberated, (approx. 5% theoretical in the case of vanillin). The use of constant-boiling hydrochloric acid in place of the hydriodic acid azeotrope therefore gives information concerning any ester groups in the molecule.

Procedure. The apparatus used is shown in Fig. 1. The sample is refluxed for 3 hours with 6 ml. constant-boiling hydrochloric acid, to which has been added approx. 0.25 g. phenol. The nitrogen carrier-gas flow-rate is 6-8 ml./min. The trapped reaction products are transferred to the appropriate gas-cell as previously described and the spectrum drawn to determine which alkyl chloride has been liberated. The peak used for calibration is drawn several times and the average peak height referred to the appropriate calibration curve obtained by Anderson's manometric technique.<sup>45</sup> An estimate of the weight of alkyl chloride released is obtained, which can be assigned to a definite number of ester groups present in the molecule, if its molecular weight is known.

If the molecule contains ester and ether groups of the same alkyl

radical, estimates of the released alkyl chloride tend to be slightly high, as a result of the very slow formation of alkyl chlorides from ether linkages.

Table 14 shows results obtained by the above method on a series of mixed ester/ether compounds.

TABLE 14

The Differentiation of Ester from Ether Groups

Compound	Mol. weight	Weight taken, mg.	% total alkoxy HI method theory		total no. of alkoxy groups	Weight taken, mg.	% ester alkoxy HCl method	No. of ester groups
Methyl-p-nitrobenzoate	181	3.28	17.0	17.1	1	10.28	16.8	1
Methyl anisate	166	1.33	37.5	37.4	2	9.41	19.2	1
Yohimbine hydrochloride	390.5	5.98	7.92	7.94	1	20.27	7.67	1
Reserpine	609	1.66	30.4	30.6	6	16.00	6.36	1
Ethyl- $\beta$ -ethoxypropionate	146	0.82	61.2	61.6	2	3.19	31.7	1
Ethyl- $\beta$ -ethoxycrotonate	158	0.98	56.6	57.0	2	2.89	29.3	1

The use of constant-boiling hydrochloric acid in the infrared method therefore gives information on the presence or absence of ester groups in the molecule. If the molecular weight of the compound is known, the number of ester groups present may be calculated, as has been done in Table 14.

Few complications have been found to occur. The method fails with

acetals and tert-butyl methoxy phenols, both of which liberate quantitative yields of alkyl chlorides in 3 hours under the hydrochloric acid treatment. The technique cannot be applied to distinguish between glycosidic and sugar ether linkages as both are cleaved and converted into methyl chloride in 3 hours. The use of more dilute acid, (1N), sufficient to hydrolyse the glycosidic link only, is not successful, since the acid is not strong enough to cause any conversion of the resulting methanol to methyl chloride.

4. Alcohols The method fails for n-propyl and n-butyl ester groups. Quantitative cleavage of the ester groups by the hydrochloric acid will undoubtedly occur, but the acid is not reactive enough to quantitatively convert the alcohols into the corresponding chlorides.

5. Alkyl Halides It is felt that the above extension of the alkoxy determination should be of use to help elucidate the structures of unknown compounds. The presence of ester groups, indicated by other qualitative methods, would be confirmed, the number and type of ester groups present in the molecule being determined by a single run using hydrochloric acid. The complete determination of the ester and ether content of a compound would take about 4 hours to complete, involving the weighing of two samples and the consumption of between 5 and 20 mg. of material.

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DEPARTMENT OF ANALYSIS OF PRODUCTS

FROM THE FRIEDRICH-AUGUST-FACILITY

LITERATURE

The Ehrlich-Sachs reaction, which was first investigated at the beginning of this century,<sup>1</sup> consists of the base-catalyzed condensation of p-ortho-N-allylamine with compounds containing a reactive carbonyl group. All condensations reported by Sachs et al.<sup>1</sup> involved the interaction of one mole of each of the reactants, but recently Bell<sup>2,3</sup> has shown that further condensation of the reactive allylic compound is very readily achieved.

PART II

Recently, Bell<sup>2,3</sup> isolated all the reaction products from typical periods of Ehrlich-Sachs reactions. The compounds were characterized by a combination of infrared spectroscopy and mass spectrometry.

THE MOLECULAR STRUCTURE OF PRODUCTS

FROM THE EHRLICH-SACHS REACTION

Compounds, strikingly similar to those given by homologous groups, were observed, and several absorptions occurring at unusual infrared frequencies were found. These features indicated that the compounds merited further examination. Analytical specimens of the various series of compounds were kindly placed at my disposal for this purpose by Professor V. Bell.

The series of compounds investigated and their collective names used hereafter in this report are outlined below.

- |                            |                                         |
|----------------------------|-----------------------------------------|
| 1. Ehrlich-Sachs Amides    | $R^1R^2N-CH_2-CH_2-C(=O)NR^3$           |
| 2. Ehrlich-Sachs Esters    | $R^1R^2N-CH_2-CH_2-C(=O)OR^3$           |
| 3. Ehrlich-Sachs Aldehydes | $R^1R^2N-CH_2-CH_2-C(=O)H$              |
| 4. Cyano-diester           | $R^1R^2N-CH_2-CH_2-C(=O)NR^3-C(=O)OR^4$ |
| 5. Mayo-ester              | $R^1R^2N-CH_2-CH_2-C(=O)OR^3$           |

where R and R' = H, Me, Et or n-Bu; R'' = H or Me; and R''' = H or n-Bu.

INTRODUCTION

The Ehrlich-Sachs reaction, which was first investigated at the beginning of this century,<sup>1</sup> consists of the base-catalysed condensation of p-nitroso-N-alkylanilines with compounds containing a reactive methylene group. All condensations described by Sachs *et al.*<sup>1</sup> involved the interaction of one mole of each of the reactants, but recent work<sup>2,3</sup> has shown that further condensation of the reactive methylene compound is very readily achieved.

Recently, Bell<sup>2,3</sup> isolated all the reaction products from typical series of Ehrlich-Sachs reactions. The compounds were characterised by a combination of infrared spectroscopy and elemental analysis. In some of the series of compounds, striking variations in the infrared absorptions given by homologous compounds were observed, and several absorptions occurring at abnormal infrared frequencies were found. These features indicated that the compounds merited further examination. Analytical specimens of the various series of compounds were kindly placed at my disposal for this purpose by Professor F. Bell.

The series of compounds investigated and their collective names used hereafter in this report are outlined below.

- |    |                           |                                                           |
|----|---------------------------|-----------------------------------------------------------|
| 1. | Ehrlich-Sachs Dinitriles: | $RR'N-\text{C}_6\text{H}_4-N:C(CN)_2$                     |
| 2. | Ehrlich-Sachs Esters:     | $RR'N-\text{C}_6\text{H}_4-N:C(CN).CO_2R'''$              |
| 3. | Ehrlich-Sachs Amides:     | $RR'N-\text{C}_6\text{H}_4-N:C(CN).CONH_2$                |
| 4. | Cyano-diesters:           | $RR'N-\text{C}_6\text{H}_4-NH.C(CO_2R'''):C(CN).CO_2R'''$ |
| 5. | Dicyano-esters:           | $RR'N-\text{C}_6\text{H}_4-NH.C(CN):C(CN).CO_2R'''$       |

where  $\underline{R}$  and  $\underline{R}'$  = H, Me, Et or n-Pr;  $\underline{R}''$  = H or Me; and  $\underline{R}'''$  = Me or Et.

EXPERIMENTAL AND DISCUSSION

A Hilger H800 infrared spectrophotometer, fitted with a rock-salt prism, was used. Calibration was effected with reference to pyrrole vapour (3530  $\text{cm.}^{-1}$ ), polystyrene film (3029 and 2925  $\text{cm.}^{-1}$ ), dichloroacetonitrile (2261  $\text{cm.}^{-1}$ ), and acetone vapours (1742  $\text{cm.}^{-1}$ ), and is believed to be accurate to  $\pm 10 \text{ cm.}^{-1}$  in the  $\text{N-H}_{\text{st}}$  absorption region,  $\pm 5 \text{ cm.}^{-1}$  in the cyano absorption region, and  $\pm 2 \text{ cm.}^{-1}$  for carbonyl absorptions. Solutions in carbon tetrachloride or in chloroform (0.005M - 0.02M) were examined in a matched pair of variable path-length cells with rock-salt windows. Solvent absorptions were removed by compensation in the reference beam. Absorptions are quoted as  $\text{cm.}^{-1}$ , which is considered a frequency.

1. Ehrlich-Sachs Dinitriles. Table 1 gives the cyano absorption frequencies of the dinitriles as solids (Nujol mull) and as 0.01M solutions in chloroform.

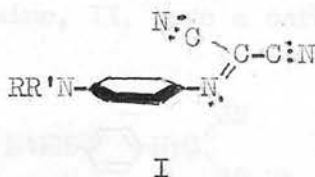
TABLE 1

Cyano Absorptions of the Series  $\text{RR}'\text{N}-\text{C}_6\text{H}_4-\text{N}(\text{R}'')\text{C}(\text{CN})_2$

R	R'	R''	C:N (mull)	C:N (solution)
Me	Me	H	2216, 2197	2227, 2212(sh)
Me	Et	H	2212, 2202(sh)	2224, 2211(sh)
Et	Et	H	2215 (1 absorption only)	2223, 2209(sh)
Me	Me	Me	2214, 2198	2221, 2210(sh)
Et	Et	Me	2214, 2198	2223, 2210(sh)

(sh) denotes shoulder.

Space-filling models of these molecules show that the two cyano groups exist in markedly different environments, one being in close conjunction with the benzene ring and inhibiting free rotation about the N-benzene ring bond, the other being remote to the ring. The least steric hindrance is given when the  $-N:C(CN)_2$  group is perpendicular to the plane of the ring, as depicted in I. The cyano group

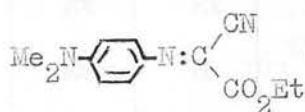


lying in close proximity to the benzene ring will be subject to interaction with the  $\pi$ -cloud of the latter, and may thus have its absorption frequency raised. Despite non-planarity of the molecule, it appears that the cyano group remote from the benzene ring can be conjugated to the latter by interaction of the benzene ring  $\pi$ -cloud, N atom lone-pair, N:C  $\pi$ -cloud and C:N  $\pi$ -cloud. It is therefore proposed that the cyano group remote from the benzene ring absorbs at  $2210 \pm 2 \text{ cm.}^{-1}$ , the cyano group in close proximity to the ring absorbing at  $2224 \pm 3 \text{ cm.}^{-1}$ . The validity of these deductions is supported by the behaviour in solution of the Ehrlich-Sachs esters discussed below.

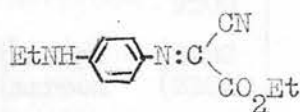
Table 1 shows that the presence of a methyl group in the 2-position of the ring, (i.e. R'' in Table 1 = Me), does not alter the absorption frequency of either cyano group, although greater steric hindrance to free rotation is created. A study of models, however, shows that the configuration which departs least from planarity and so has the greatest stability is given when the cyano group and the hydrogen atom in the 6-position are in close proximity. The preferred molecular configuration will therefore not be changed by substitution of a methyl

group in the 2-position. This effect also applies to the other series of compounds discussed in this report, and will not be further mentioned.

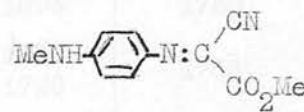
2. Ehrlich-Sachs Esters. In this series, striking variations in the carbonyl absorptions of the solids were observed. Thus, N-(~~α~~-cyano-~~α~~-ethoxycarbonylmethylene)-N,N'-dimethyl-p-phenylenediamine, II, gave a carbonyl absorption at 1740  $\text{cm.}^{-1}$ ,



II



III



IV

whereas its methoxy analogue absorbed at 1708  $\text{cm.}^{-1}$ . Moreover, N-(~~α~~-cyano-~~α~~-ethoxycarbonylmethylene)-N'-ethyl-p-phenylenediamine, III, existed in two crystalline modifications -- (a) maroon prisms, m.p. 107°C.,  $\nu_{\text{C=O}}$  1726  $\text{cm.}^{-1}$ , and (b) orange needles, m.p. 107°C.,  $\nu_{\text{C=O}}$  1750  $\text{cm.}^{-1}$ , both from ethanol; N-(~~α~~-cyano-~~α~~-methoxycarbonylmethylene)-N'-methyl-p-phenylenediamine, IV, existed in three crystalline modifications -- (a) maroon needles, m.p. 170°C., from methanol,  $\nu_{\text{C=O}}$  1687  $\text{cm.}^{-1}$ , (b) yellow-orange needles, m.p. 170°C., from benzene,  $\nu_{\text{C=O}}$  1713  $\text{cm.}^{-1}$ , and (c) dark red prisms with blue fract, m.p. 168°C., from the benzene mother liquor,  $\nu_{\text{C=O}}$  1735 and 1706  $\text{cm.}^{-1}$ . Table 2 lists the cyano and carbonyl absorption frequencies of the esters as mulls and as 0.005M solutions in carbon tetrachloride.

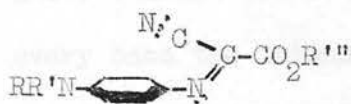
The marked variations in both the carbonyl and cyano absorption frequencies given by mulls disappeared when the compounds were studied in solution, when two carbonyl bands were given. The low and constant single absorption ( $2211 \pm 5 \text{ cm.}^{-1}$ ) of the cyano group indicated, in terms of the deduction already made concerning

TABLE 2

Cyano and Carbonyl Absorptions of the Series  $RR'N-\text{C}_6\text{H}_4-N:C(CN).CO_2R''$

R	R'	R''	R'''	C:N		C:O		
				Mull	Soln.	Mull	Soln.	
Me	Me	H	Me	2220	2212	1708	1757,	1731
Me	Me	H	Et	2200	2213	1740	1754,	1724
Et	Et	Me	Et	2200	2207	1694	1750,	1722
Et	H	H	Et	(orange maroon 2220 2202)	2211	(1750 1726)	1756,	1726
Me	H	H	Me	(orange maroon 2210 2198)	2216	(1713 1687)	1760,	1733
Et	H	H	Me	2210	2214	1731	1760,	1733
Me	H	H	Et	2215	2216	1741	1756,	1727

cyano groups, that, of the two possible geometrical isomers, V and VI, the latter is preferentially formed under the reaction conditions used.<sup>2</sup>



V



VI



VII

The occurrence of a single carbonyl frequency in the solids and of two in the solutions is clear evidence that the molecules can exist as rotational isomers, as represented by VI and VII.

Models show that, due to the ester group, free rotation about the N-benzene ring bond is inhibited. However, in the position of least hindrance, rotation can take place about the C-CO<sub>2</sub>R''' bond. In VI, the carbonyl group is in

close proximity to the  $\pi$ -cloud of the benzene ring, and the resultant negative-negative interaction will suppress the polarisation of the keto group and raise the carbonyl frequency. (An  $\alpha$ -activated,  $\alpha\beta$ -unsaturated ester would be expected<sup>4</sup> to give absorption in the range 1735 - 1750  $\text{cm.}^{-1}$ ). The above interaction should raise the carbonyl frequency by some 10 - 20  $\text{cm.}^{-1}$ , so the assignment of  $1755 \pm 5 \text{ cm.}^{-1}$  to the carbonyl absorption of conformation VI is made. In VII, the OR'' group is in close proximity to the benzene ring  $\pi$ -cloud. This will result in an increased contribution from the polar canonical form  $\text{R}''\text{O}^+:\text{C}=\text{O}^-$  to the carbonyl absorption. This resonance form may be further stabilised by interaction of the opposed formal charges on the carbonyl oxygen atom and the closely adjacent carbon atom of the cyano group. Thus the carbonyl frequency of isomer VII should be considerably lower than in VI; the assignments of  $1755 \pm 5 \text{ cm.}^{-1}$  and  $1725 \pm 5 \text{ cm.}^{-1}$  can be made to VI and VII respectively.

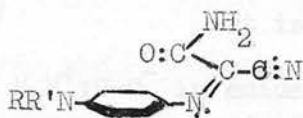
Temperature dependence measurements were made to investigate the relative stabilities of the two isomers VI and VII for each member of the series. In every case the intensity of absorption of the  $1725 \text{ cm.}^{-1}$  band increased with temperature increase. Isomer VII is therefore the less stable form.<sup>5</sup> The fact that the more stable form is that in which the opposition of like charges is greatest has been previously discussed,<sup>5</sup> but is apparently not yet fully understood.

The variations in the carbonyl absorptions of the solids can be attributed to the fixation of one or other isomer, consistent with the production of the lattice of lowest energy. Two of the compounds studied were isolated in different crystal forms having different infrared spectra as solids (see Table 2). Use of a Kofler hot-stage microscope showed that, in each case, one of the forms was unstable, having a transition temperature below the true melting point at which

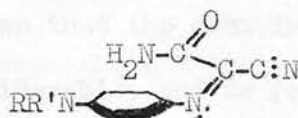
it irreversibly changed, accompanied by a change in colour and crystal structure, to the more stable crystallographic form. Thus the maroon form of N-( $\alpha$ -cyano- $\alpha$ -ethoxycarbonylmethylene)-N'-ethyl-p-phenylenediamine, <sup>III,</sup><sub>A</sub> changed at 86°C. to the orange form (m.p. 107°C.); for N-( $\alpha$ -cyano- $\alpha$ -methoxycarbonylmethylene)-N'-methyl-p-phenylenediamine, IV, the orange form changed at 158°C. to the maroon form (m.p. 170°C.). Infrared studies of the temperature dependence of these two compounds showed that, at the transition temperature, two carbonyl bands were given, one of which slowly decreased in intensity as the temperature was gradually raised, finally leaving the other as a single band. When the compound finally melted, the two bands reappeared.

These examples of rotational isomerism support the initial assignments of the cyano frequencies in the Ehrlich-Sachs dinitriles. If the assignments be reversed, leading to V in place of VI, models show that, although rotational isomerism of the ester group is still possible, an explanation of the large differences in the two carbonyl absorptions can no longer be found.

3. Ehrlich-Sachs Amides. Table 3 lists the cyano absorption frequencies and the absorption frequencies of bands in the carbonyl region of the amides, as mulls and as 0.01M solutions in chloroform. All <sup>solutions</sup> exhibited a cyano band at  $2211 \pm 3 \text{ cm.}^{-1}$ . The assignment for cyano groups therefore favours the structure VIII, or its



VIII



IX



X

possible rotational isomer IX, rather than X. In the carbonyl absorption region

TABLE 3

## Cyano Absorptions and Absorptions in the Carbonyl

Region of the Series  $RR'N-\overset{R''}{\text{C}_6\text{H}_4}-N:C(CN).CONH_2$ 

R	R'	R''	C:N		C:O region				
			Mull	Soln.	Mull		Soln.		
Me	Me	H	2200	2210	1682,	1616	1692,	1615	
Et	Et	H	2202	2213	1680,	1613	1693,	1614	
n-Pr	n-Pr	H	2202	2214	1716,	1660,	1615	1694,	1616
Me	Me	Me	2200	2209	1680,	1614	1696,	1615	
Et	Et	Me	2202	2213	1684,	1614	1696,	1616	

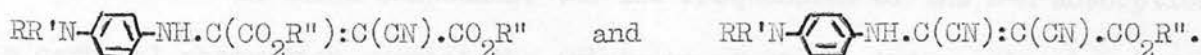
bands were present at  $1694 \pm 2$  (s) and  $1615 \pm 1$  (s). When each compound was studied in a range of solvents of varying polarity, the  $1694 \text{ cm.}^{-1}$  band varied between  $1710 \text{ cm.}^{-1}$  ( $\text{CCl}_4$ ) and  $1691 \text{ cm.}^{-1}$  ( $\text{CHBr}_3$ ), whilst the  $1615 \text{ cm.}^{-1}$  band remained constant. A  $d\nu/\nu$  plot (based on carbon tetrachloride) for the  $1691 - 1710 \text{ cm.}^{-1}$  band against acetophenone<sup>6</sup> gave a straight line. Hence only one carbonyl band is given in solution, the  $1615 \text{ cm.}^{-1}$  band being attributed to the N:C bond. Rotational isomerism, although perfectly feasible on steric grounds, is therefore not exhibited by these amides.

It is well known that the contribution of the polar canonical form  $H_2N^+ : C=O^-$  in amides is considerable, and is responsible<sup>4</sup> for the carbonyl absorption normally occurring in dilute solution near  $1690 \text{ cm.}^{-1}$ . An  $\alpha$ -activated,  $\alpha\beta$ -unsaturated amide would also be expected to give a carbonyl band near  $1690 \text{ cm.}^{-1}$ . The observed  $1691 - 1710 \text{ cm.}^{-1}$  band therefore indicates that an activation effect on the carbonyl

group is tending to reduce the  $H_2N^+ : C-O^-$  contribution. This effect would be given in structure VIII, on the basis of the same reasoning given in the discussion on Ehrlich-Sachs esters. Structure IX would lead to increased contribution by the form  $H_2N^+ : C-O^-$ , leading to an absorption frequency much lower than that normally exhibited by amides. It is concluded that in structure IX the charge distribution effects become so great that the isomer is unstable.

The compound N-carbamoylcyanomethylene-N'N'-di-n-propyl-p-phenylenediamine was, however, found to give two carbonyl bands at  $1714\text{ cm.}^{-1}$  (w) and  $1657\text{ cm.}^{-1}$  (s) in the solid state (see Table 3). In the liquid state and in chloroform solution only one band at  $1694\text{ cm.}^{-1}$  was given. Repeated purification procedures failed to yield material from which the  $1714\text{ cm.}^{-1}$  band was absent in the solid state. Identical spectra were given by crystals grown from different solvents and from cast films: the possibility of the presence of dimorphic crystal forms is therefore small. The cause of this effect was not determined. A similar crystal effect was given by the compound N-( $\alpha$ -cyano- $\alpha$ -methoxycarbonylmethylene)-N'-methyl-p-phenylenediamine, IV; on one occasion a strongly crystalline isomer was isolated, which gave two carbonyl absorptions at  $1733\text{ cm.}^{-1}$  (m) and  $1706\text{ cm.}^{-1}$  (m) in the solid state. On melting, the compound crystallised as the stable yellow-orange isomer, giving absorption at  $1713\text{ cm.}^{-1}$ . Numerous recrystallisation attempts failed to yield any further quantity of the isomer, which would appear to have been formed by the simultaneous crystallisation of both rotational isomers.

4 and 5. Cyano-diesters and Dicyano-esters. Infrared evidence suggested<sup>5</sup> that these compounds contained an N-H group and were of general formulae



The presence of an N-H group has been confirmed by alkaline hydrolysis to the corresponding NN-dialkyl-p-phenylenediamines, which were characterised by conversion to their acetyl and benzoyl derivatives.<sup>7</sup>

The compounds were studied as mulls and as 0.01M solutions in carbon tetrachloride, methylene chloride, chloroform, diethyl ether, nitromethane and bromoform. For each compound, both the solid and solution absorptions given were remarkably constant, as shown in Table 4. Twelve compounds in all were studied, that is, all possible combinations of R, R', and R'' = Me and Et.

TABLE 4

Solid and Solution Spectra of the Series

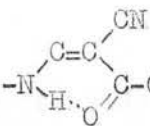
(a)  $RR'N-\text{C}_6\text{H}_4-\text{NH}\cdot\text{C}(\text{CO}_2\text{R}'')$ : $\text{C}(\text{CN})\cdot\text{CO}_2\text{R}''$  and (b)  $RR'N-\text{C}_6\text{H}_4-\text{NH}\cdot\text{C}(\text{CN})$ : $\text{C}(\text{CN})\cdot\text{CO}_2\text{R}''$


N-H			C:N		C:O					
Mull*	Soln.*	Solvent variation.†	Mull*	Soln.*	Mull*	Soln.*	Solvent variation.†	Mull*	Soln.*	Solvent variation.†
a) 3275±20	3215±10	±5	2228±8	2222±5	1755±5	1755±5	±7	1675±5	1675±5	±2
b) 3235±35	3220±20	±10	2222±12	2220±5 (1 band only)	---	---	--	1688±6	1678±6	±3


\*  $\pm x$  = limits of variation of the band between compounds in the series as solids (Mull) and in carbon tetrachloride solution. (Soln.)

†  $\pm y$  = maximum variation of the band of each compound in solvents of differing polarities.

In these compounds, the low frequencies of the N-H absorption and of a carbonyl absorption suggest the existence of strong intra-molecular hydrogen-bonding.

Models show that the  group forms a compact six-membered ring system, and the frequency 1675 cm.<sup>-1</sup> is therefore assigned to this ester group. The variation of this band in different solvents was very small, ±3 cm.<sup>-1</sup> (Table 4). This is consistent with strong intra-molecular hydrogen-bonding which prevents normal interaction of proton donating solvents with the C:O bond.<sup>8</sup> The second ester group (1755 cm.<sup>-1</sup>) in the cyano-diester (series (a) in Table 4) suffers severe steric hindrance and is almost 90° out of plane with respect to the C:C bond. The absorption frequency observed is therefore more typical of a saturated, α-activated ester, than of an α-activated, β-unsaturated ester. It is of interest that Felton and Orr<sup>9</sup> have reported frequencies of ~1750 cm.<sup>-1</sup> for severely hindered β-unsaturated esters.

The Cause of the High Colour of the Dicyano-esters. These compounds lack extended conjugation but are dark red in colour. The corresponding cyano-diester are all pale yellow, due to an absorption band in the ultraviolet region (~560 mμ) extending into the visible spectrum. Solutions of the dicyano-esters in chloroform showed a broad band with λ<sub>max</sub> ~ 450 mμ. A study of very dilute solutions (5x10<sup>-4</sup>M - 5x10<sup>-5</sup>M) of Et<sub>2</sub>N--NH.C(CN):C(CN).CO<sub>2</sub>Et in chloroform in 1 - 10 mm. quartz cells showed that the intensity of the 453 mμ band decreased rapidly with decreasing concentration, whilst a new band (λ<sub>max</sub> = 546 mμ) increased in intensity. The spectra exhibited an isosbestic point at 594 mμ, and so it was concluded that there were two species present in solution.

To investigate this effect, a series of tricyanovinylanilines, R--NH.C(CN):C(CN)<sub>2</sub>, was prepared,<sup>7</sup> where R = H, Me, Et, iso-Pr, tert-Bu, OMe and NMe<sub>2</sub>. The series, therefore, had increasing electron donation from the R-groups in the para-position. The series ranged in colour from very pale yellow for R = H

to orange for R = OMe, but the R = NMe<sub>2</sub> compound was deep maroon. The yellow series had  $\lambda_{\max}$  ranging from 548 m $\mu$  for R = H to 562 m $\mu$  for R = OMe ( $5 \times 10^{-4}$  M solutions in chloroform); this absorption is clearly due to the simple molecule. For p-NN-dimethyltricyanovinylaniline, however, the visible band ( $\lambda_{\max} = 445$  m $\mu$ ) decreased with decreasing concentration in very dilute solutions ( $5 \times 10^{-4}$  M -  $5 \times 10^{-6}$  M) in chloroform) whilst a band at 370 m $\mu$  simultaneously increased. An isosbestic point occurred at 403 m $\mu$ . In this case also, therefore, two species were present in solution. The anomalous deep colour of p-NN-dimethyltricyanovinylaniline and of the series of dicyano-esters may therefore be attributed to some form of self- $\pi$ -complexing arising from the particular molecular structure. The complex is destroyed at very high dilutions, with liberation of the simple molecules, which absorb in the anticipated region of the ultraviolet.

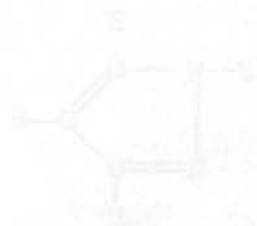
All ultraviolet and visible spectroscopic measurements were performed on a Unicam S.P.500 ultraviolet and visible spectrophotometer, using 1, 2, 10, 20, and 40 mm. Unicam quartz cells. Chloroform, specially purified for spectroscopy, was used as solvent.

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INTRODUCTION

Bickel *et al.*<sup>1</sup> have exhaustively measured the main physical properties of pyrazole (I) and imidazole (II). They concluded that in non-polar



(I)



(II)

PART III

solvents both compounds exhibited hydrogen bonding, and that pyrazole existed as an equilibrium mixture

THE HYDROGEN BONDING OF SIMPLE HETEROCYCLIC  
MOLECULES IN CARBON TETRACHLORIDE SOLUTION

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(III)

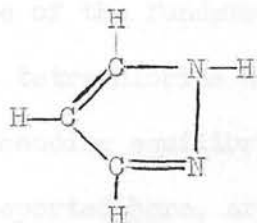


(IV)

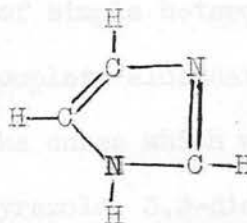
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INTRODUCTION

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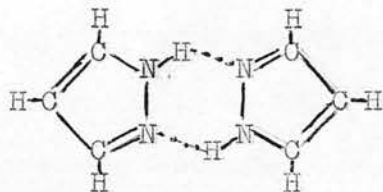


(I)

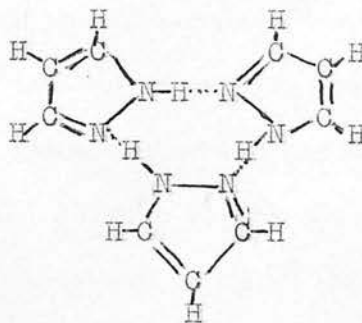


(II)

solvents both compounds exhibited hydrogen bonding, and that pyrazole existed as an equilibrium mixture of monomer and cyclic dimer, with higher linear oligomers at high concentrations, while imidazole existed as an infinite series of linear oligomers. The case of imidazole has never been questioned, the formation of small, cyclic, hydrogen-bonded species being rendered impossible by the relative positions of the two nitrogen atoms in the ring. The validity of Hückel's conclusions for the hydrogen bonding of pyrazole has, however, been questioned by Hunter,<sup>2</sup> who criticised the non-linearity of the hydrogen bonds in the dimer (III) and proposed that the strainless cyclic trimer (IV) should be a more stable



(III)



(IV)

hydrogen-bonded configuration. Some confirmatory evidence of this proposal has

come from a cryoscopic study of 3,5-dimethylpyrazole in benzene by White and Kilpatrick,<sup>5</sup> who obtain convincing evidence for the existence of a stable cyclic trimer and dubious evidence for an unstable, and probably linear, dimer.

It was considered that the detailed analysis of the concentration dependence of the fundamental N-H stretching band of simple heterocyclic molecules in carbon tetrachloride solution could lead to a complete elucidation of the hydrogen bonding equilibria of these molecules. The cases which were considered, and are reported here, are pyrazole, 3,5-dimethylpyrazole, 3,5-diethylpyrazole, 3,5-diphenylpyrazole, and imidazole.

EXPERIMENTAL

Materials. Pyrazole, 3,5-dimethylpyrazole and imidazole were all commercial samples. The former two were recrystallised twice from cyclohexane before use; imidazole was recrystallised twice from carbon tetrachloride. The melting points of all three purified compounds agreed with those given in the literature. 5,5-diphenylpyrazole was prepared by direct condensation of equimolar amounts of dibenzoylmethane and hydrazine hydrate in ethanol. The product was recrystallised twice from carbon tetrachloride and had a m. p. of 199-200° (lit. 200°). 3,5-diethylpyrazole was prepared similarly from dipropionylmethane, (prepared by the method of Zellars and Levine<sup>4</sup>), and was purified by distillation under reduced pressure. It was a colourless solid of m. p. 23-24° (lit. 22-24°).

Reagent grade carbon tetrachloride was used as solvent without further purification. Using 4 cm. cells it gave no detectable infrared absorption in the region examined, 4000-2400 cm.<sup>-1</sup>

Infrared Measurements. A Hilger H800 double beam infrared spectrometer, fitted with a quartz prism, was used. The quartz prism gave a theoretical slit-width of 8 cm.<sup>-1</sup> at 5500 cm.<sup>-1</sup> with a spectrometer slit-width of 0.50 mm. The frequency scale was calibrated with reference to the N-H stretching frequency of pyrrole vapour (3530 cm.<sup>-1</sup>) and the C-H stretching frequencies of polystyrene film (3029 and 2925 cm.<sup>-1</sup>). The spectrometer was not thermostatted and wave-number estimates are considered to be accurate to  $\pm 10$  cm.<sup>-1</sup> within the region 3500-2800 cm.<sup>-1</sup> Run-to-run reproducibility was  $\pm 5$  cm.<sup>-1</sup> The instrumental conditions were: gain, 4; damping, 2; speed of scan, 68 cm.<sup>-1</sup>/min. For absorption measurements carefully matched pairs of 4.00, 2.00 and 1.00 cm. Unicam quartz cells

were used, while for the most concentrated solutions a pair of variable path-length cells, set at  $5.000 \pm 0.005$  mm., and fitted with rock-salt windows, were used.

The instrument was operated with pure solvent in the reference beam.

The studies on the hydrogen bonding equilibria of each compound will be treated separately. Each section will contain its own experimental procedure, interpretation of the data, and discussion.

Table I-1 Absorption Bands of Pyrazole

State	3175	3080	2950	2800	2660	2100 (shoulder)
Solid (neat film)						
$CCl_4$ solution						

(all peaks strong)

An X-ray analysis has shown that pyrazole exists in the solid state as long, parallel, hydrogen-bonded chains, which describe figure-of-eight spirals. The hydrogen bonds are linear. It appeared inconceivable that a cyclic trimer, with strained hydrogen bonds, could give an identical band spectrum to a strainless spiral. The strainless cyclic trimer, however, is a much closer representation of the spiral, since opening the ring and rotating the pyrazole molecule through  $180^\circ$  gives the band pattern of the spiral. It might therefore be expected that a cyclic trimer and the spiral would have very closely similar band K-O absorptions.

A quantitative study of the concentration dependence of the 3175 cm<sup>-1</sup> band was therefore made to determine the nature of the pyrazole oligomers in carbon tetrachloride solution.

THE HYDROGEN BONDING OF PYRAZOLE IN CARBON TETRACHLORIDE SOLUTION

A preliminary study of dilute solutions of pyrazole in carbon tetrachloride showed a fundamental N-H stretching mode at  $3485 \pm 5 \text{ cm.}^{-1}$  with a half-band width of  $20 \text{ cm.}^{-1}$ . The intensity of this band decreased with increasing total concentration, B; concurrently, a broad, bonded N-H band of increasing intensity appeared in the region  $3400\text{-}2000 \text{ cm.}^{-1}$  (see Fig. 1). This broad band showed six major peaks (excluding that due to C-H at  $3120 \text{ cm.}^{-1}$  (w)) which were remarkably similar to the infrared N-H absorption of a solid, cast film of pyrazole.

Bonded N-H Absorption Bands of Pyrazole

Solid (cast film)	3135	3050	2960	2900	2860	2810(shoulder)
$\text{CCl}_4$ solution	3175	3070	2995	2930	2905	2825(shoulder)

(all peaks strong)

An X-ray analysis<sup>5</sup> has shown that pyrazole exists in the solid state as long, parallel, hydrogen-bonded chains, which describe figure-of-eight spirals. The hydrogen bonds are linear. It appeared incompatible that a cyclic dimer, with strained hydrogen bonds, could give an identical bonded N-H spectrum to a strainless spiral. The strainless cyclic trimer, however, is a much closer representation of the spiral, since opening the ring and rotating one pyrazole molecule through  $180^\circ$  gives the basic pattern of the spiral. It might therefore be expected that a cyclic trimer and the spiral would have very closely similar bonded N-H absorptions.

A quantitative study of the concentration dependence of the  $3485 \text{ cm.}^{-1}$  band was therefore made to determine the nature of the pyrazole oligomers in carbon tetrachloride solution.

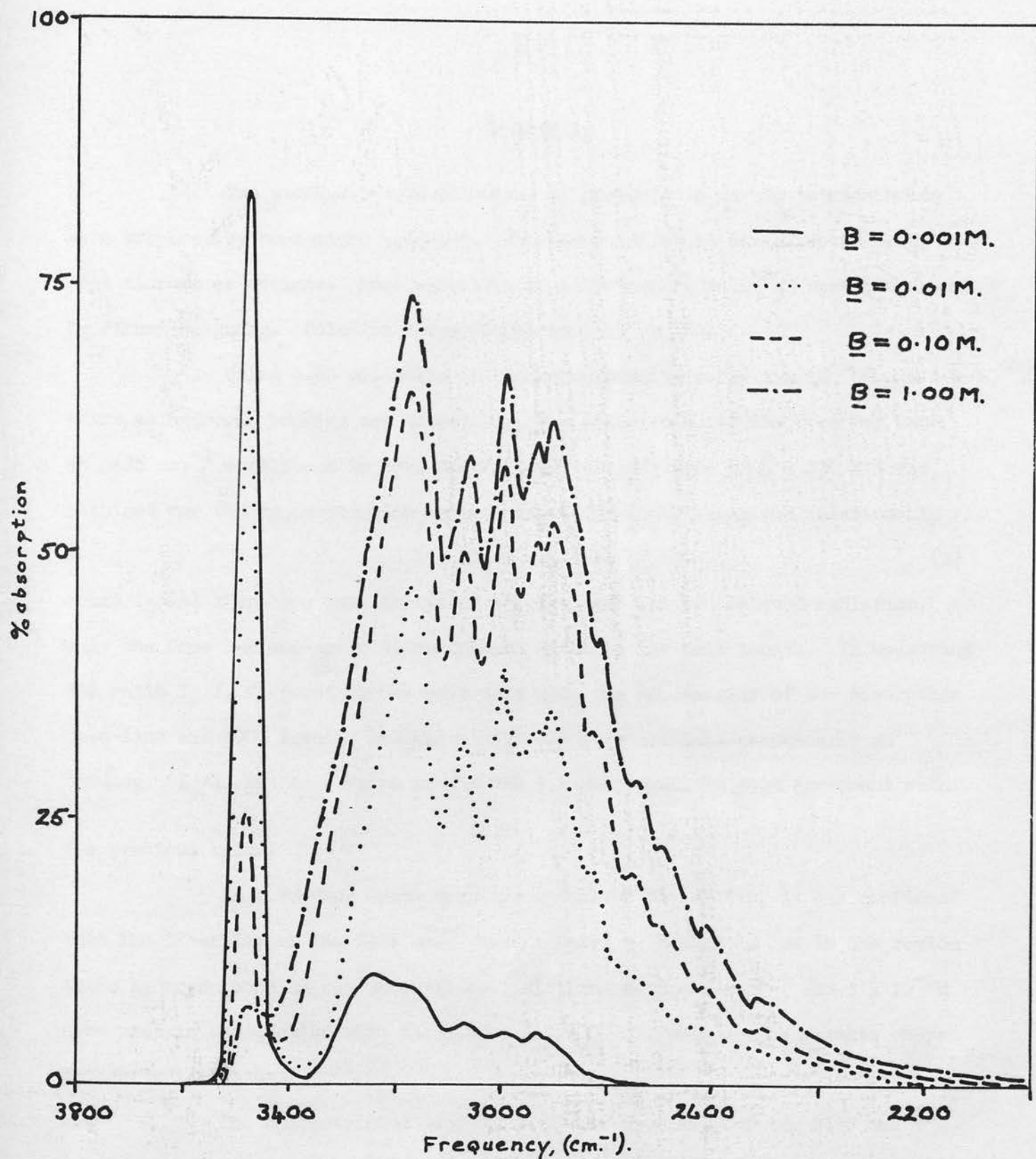


Fig. 1. Infrared absorption spectra in the region 3800-2000 cm<sup>-1</sup> for carbon tetrachloride solutions of pyrazole at various total concentrations,  $\underline{B}$ , at 18° C.

Procedure

Two stock 0.09947M solutions of pyrazole in carbon tetrachloride were prepared by semi-micro weighing. Subsequent dilution was effected using an Agla micrometer syringe. More concentrated solutions ( $\underline{B} > 10^{-1}M$ ) were prepared by direct weighing. Solution temperatures were  $18^{\circ} \pm 1^{\circ}C$ .

Using 4.00 cm. cells in the concentration range  $1 \times 10^{-4} \leq \underline{B} \leq 4 \times 10^{-4}M$ , where no hydrogen bonding was detectable, the intensities of the free N-H band at  $3485 \text{ cm.}^{-1}$  were found to obey Beer's law. A mean value of  $\underline{\epsilon} = 220 \pm 3$  was obtained for the apparent molar extinction coefficient, using the relationship

$$\log (I_0/I) = \underline{\epsilon}el \quad (1)$$

where  $I_0$  and  $I$  are the intensities of the incident and transmitted radiation,  $e$  is the free N-H end-group concentration and  $l$  is the cell length. In measuring the ratio  $I_0/I$ , frequent checks were made upon the constancies of the absorption base-line and 100% level. The value of  $\underline{\epsilon}$  was also obtained graphically as

$\lim_{\underline{B} \rightarrow 0} (\log (I_0/I)/\underline{B}l)$  : a value of  $\underline{\epsilon} = 220 \pm 2$  was found, in good agreement with

the previous value.

As a further check upon the optics of the system, it was confirmed that the intensity of the  $3485 \text{ cm.}^{-1}$  band adhered to Lambert's law in the region where hydrogen bonding was detectable. Solutions of  $\underline{B} = 8 \times 10^{-4}$  and  $1 \times 10^{-3}M$  were used in conjunction with the 4.00 and 0.5000 cm. cells. The results obeyed Lambert's law to  $\pm 1\%$ .

The concentration dependence of the intensity of the  $3485 \text{ cm.}^{-1}$  band was then studied. Forty-three solutions ( $10^{-4} \leq \underline{B} \leq 10^{-2}M$ ) were prepared in duplicate, one from each stock solution. Intensities were reproducible to  $\pm 1\%$ , and the mean absorbancies are given in Table 1, together with the end-group concentrations,  $e$ , calculated therefrom.

TABLE 1

Infrared Absorbancies at 3485 cm.<sup>-1</sup> of Associated Pyrazole  
in Carbon Tetrachloride at 18° ± 1°C

10 <sup>4</sup> $\underline{B}$	0.9947	1.989	2.984	3.979	4.974	5.968	6.963	7.958	8.952
log I <sub>0</sub> /I	0.0894*	0.174*	0.260*	0.347*	0.417*	0.494*	0.574*	0.646*	0.721*
10 <sup>4</sup> e	--	--	--	--	4.736	5.608	6.517	7.340	8.195
10 <sup>4</sup> $\underline{B}$	9.947	11.94	13.95	15.92	17.91	19.89	21.88	23.87	25.86
log I <sub>0</sub> /I	0.099	0.118	0.134	0.150	0.167	0.179	0.193	0.210	0.222
10 <sup>4</sup> e	8.954	10.68	12.15	13.64	15.17	16.28	17.50	19.06	20.16
10 <sup>4</sup> $\underline{B}$	27.85	29.84	31.83	33.82	35.81	37.80	39.79	41.78	43.77
log I <sub>0</sub> /I	0.235	0.244	0.257	0.271	0.287	0.295	0.305	0.314	0.329
10 <sup>4</sup> e	21.37	22.19	23.32	24.62	26.05	26.82	27.76	28.57	29.89
10 <sup>4</sup> $\underline{B}$	45.76	47.75	49.74	51.72	53.71	55.70	57.69	59.68	61.67
log I <sub>0</sub> /I	0.336	0.346	0.351	0.363	0.373	0.385	0.394	0.399	0.408
10 <sup>4</sup> e	30.57	31.44	31.88	32.95	33.87	35.01	35.78	36.17	37.07
10 <sup>4</sup> $\underline{B}$	63.66	65.65	67.64	69.63	79.58	89.52	99.47		
log I <sub>0</sub> /I	0.419	0.426	0.434	0.438	0.478	0.507	0.539		
10 <sup>4</sup> e	38.10	38.73	39.47	39.79	43.42	46.11	49.01		

\* 4.00 cm. cells; all other results refer to 0.5000 cm. cells.

Interpretation of the Data.

It cannot be assumed a priori that the free N-H band at 3485 cm.<sup>-1</sup> in associated pyrazole solutions is due to the monomer only.<sup>6,7</sup> It is, however, valid to assume that the band is due to free N-H end-groups, and, further, that the apparent molar extinction coefficients of all linear oligomers B<sub>q</sub> are equal. End-group concentrations, e, were therefore calculated using the experimental value of  $\epsilon = 220 \pm 3$  for the monomer (see Table 1). Overall association constants are defined as

$$\beta_{q0} = \frac{B_q}{b^q} \quad (2)$$

where  $\frac{B_q}{b^q}$  is the concentration of the species B<sub>q</sub>, and b the concentration of the monomer. Anticipating our conclusions by limiting subsequent consideration to monomeric, dimeric and trimeric species, two mass balance expressions follow from

eqn. (2): 
$$\underline{B} = B_1 + 2B_2 + 3B_3 = b + 2\beta_{20}b^2 + 3\beta_{30}b^3 \quad (3)$$

$$\underline{S} = B_1 + B_2 + B_3 = b + \beta_{20}b^2 + \beta_{30}b^3 \quad (4)$$

where  $\underline{S}$  is the sum of the concentrations of all species.

It was found that the experimental data could be represented by the linear equation

$$(\underline{B} - e)/e^2 = 22,620e + 94.8 \quad (5)$$

with standard deviations in the slope and intercept of  $\pm 716$  and  $\pm 2$  respectively, found by an unweighted least squares treatment. The significance of the experimental eqn. (5) follows from a consideration of the four possible combinations of linear and cyclic oligomers, B<sub>2</sub> and B<sub>3</sub>. The experimental variables  $(\underline{B} - e)/e^2$  and e are expressed in terms of b using eqns. (3) and (4) for the four possibilities in Table 2.

TABLE 2

The Possible Variables of eqn. (5) for the Pyrazole System in Carbon Tetrachloride

$B_2$	$B_3$	$(B - e)/e^2$	$e$
cyclic	cyclic	$2\beta_{20} + 3\beta_{30}b$	$b$
linear	linear	$(\beta_{20} + 2\beta_{30}b)/(1 + \beta_{20}b + \beta_{30}b^2)^2$	$b + \beta_{20}b^2 + \beta_{30}b^3$
cyclic	linear	$(2\beta_{20} + 2\beta_{30}b)/(1 + \beta_{30}b^2)^2$	$b + \beta_{30}b^3$
linear	cyclic	$(\beta_{20} + 3\beta_{30}b)/(1 + \beta_{20}b)^2$	$b + \beta_{20}b^2$

It is apparent that eqn. (5) will be linear if the free N-H band is in fact due to monomeric pyrazole only, and the dimer and trimer are both cyclic. It is extremely unlikely that a linear representation of the data according to eqn. (5) would have been found if either or both the associated species were linear. Values of

$$\beta_{20} = 47.4 \pm 1.0 \text{ l. mole}^{-1} \text{ and } \beta_{30} = 7540 \pm 240 \text{ l.}^2 \text{ mole}^{-2}$$

were therefore derived from eqn. (5).

The values of the association constants were checked by the curve-fitting method suggested by Rossotti and Rossotti.<sup>8</sup> For systems which may be described in terms of the formation of a dimer and trimer only, eqn. (5) may be written as

$$\log\{(B - b)/b^2\} - \log 2\beta_{20} = \log \{1 + (3\beta_{30}b/2\beta_{20})\} \quad (6)$$

Substitution of the normalised variables defined by

$$\log F_m = \log F - \log 2\beta_{20} \quad (7)$$

where  $F = (B - b)/b^2$ , and

$$\log b_m = \log b + \log (3\beta_{30}/2\beta_{20}) \quad (8)$$

into eqn. (6) gives

$$\log \frac{F}{m} = \log (1 + \frac{b}{m}) \quad (9)$$

The experimental data  $\log F = \log \left\{ \frac{(B - b)}{b^2} \right\}$  plotted as a function of  $\log b$  will therefore be of the same shape as the normalised curve  $\log \frac{F}{m} = \log (1 + \frac{b}{m})$  plotted as a function of  $\log b$ . The experimental and normalised curves were

superimposed, and, in the position of best fit (see Fig. 2), the equations

$$\log \frac{F}{m} = \log (1 + \frac{b}{m}) = \log \left\{ \frac{(B - b)}{b^2} \right\} - \log 2\beta_{20} \quad (7)$$

and

$$\log \frac{b}{m} = \log b + \log (3\beta_{30}/2\beta_{20}) \quad (8)$$

were solved for  $\beta_{20}$  and  $\beta_{30}$ . The permissible relative displacements of the experimental and normalised curves, parallel to the coordinate axes, gave estimates of the errors in the two parameters. Hence, values of

$$\beta_{20} = 47.5 \pm 1.0 \text{ l. mole}^{-1} \text{ and } \beta_{30} = 7,540 \pm 300 \text{ l.}^2 \text{ mole}^{-1}$$

were obtained, in excellent agreement with the values obtained from the linear equation. This treatment therefore confirmed that monomer, cyclic dimer and cyclic trimer were the only species coexisting in the concentration range  $10^{-4} \leq B \leq 10^{-2} \text{ M}$ . There was no evidence for detectable concentrations of larger oligomers.

### Discussion

The percentage distribution of pyrazole between the monomer, cyclic dimer and cyclic trimer has been calculated as a function of the total concentration of pyrazole using eqn. (3), and is shown in Fig. 3. The precise infrared measurements from which the equilibria have been deduced only extend up to  $B = 10^{-2} \text{ M}$ ,

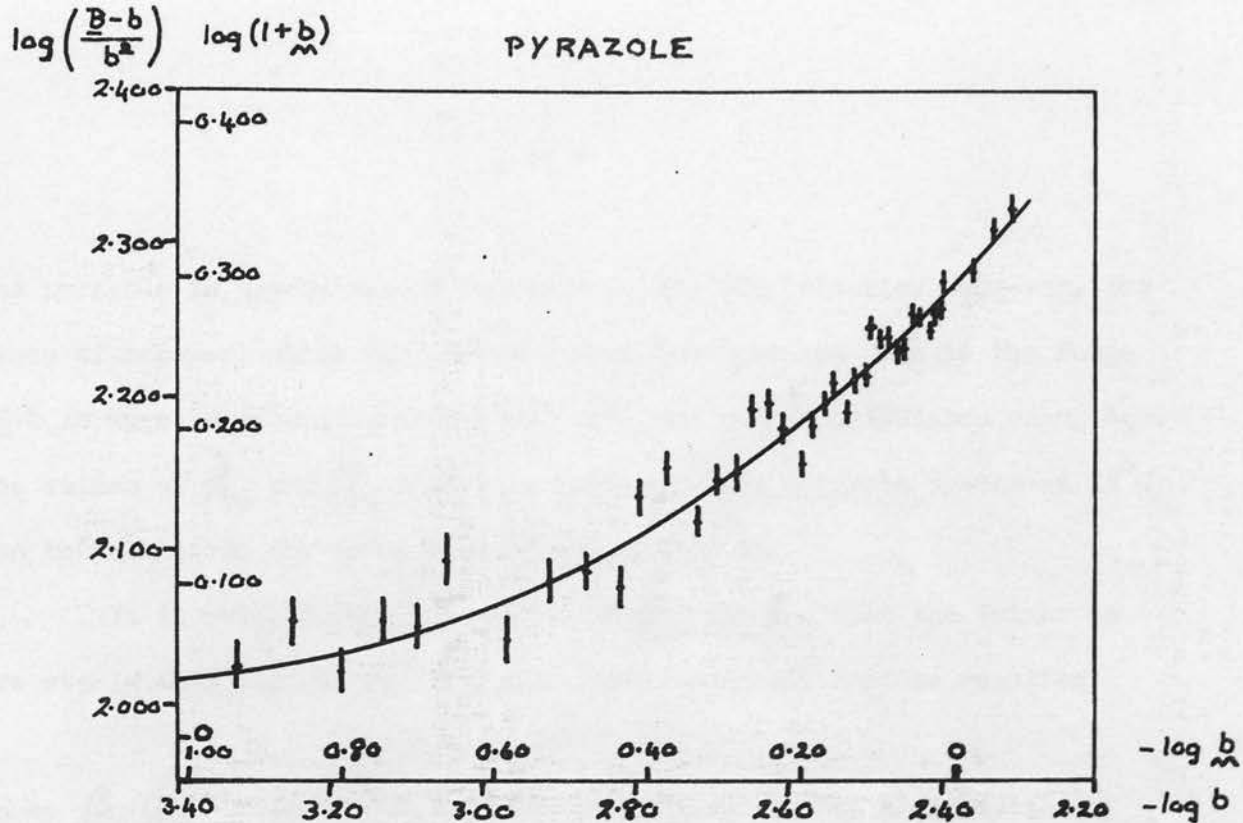


Fig. 2. The experimental data  $\log[(B-b)/b^2] : \log b$  superimposed in the position of best fit on the normalised curve  $\log(1+b) : \log b$ .

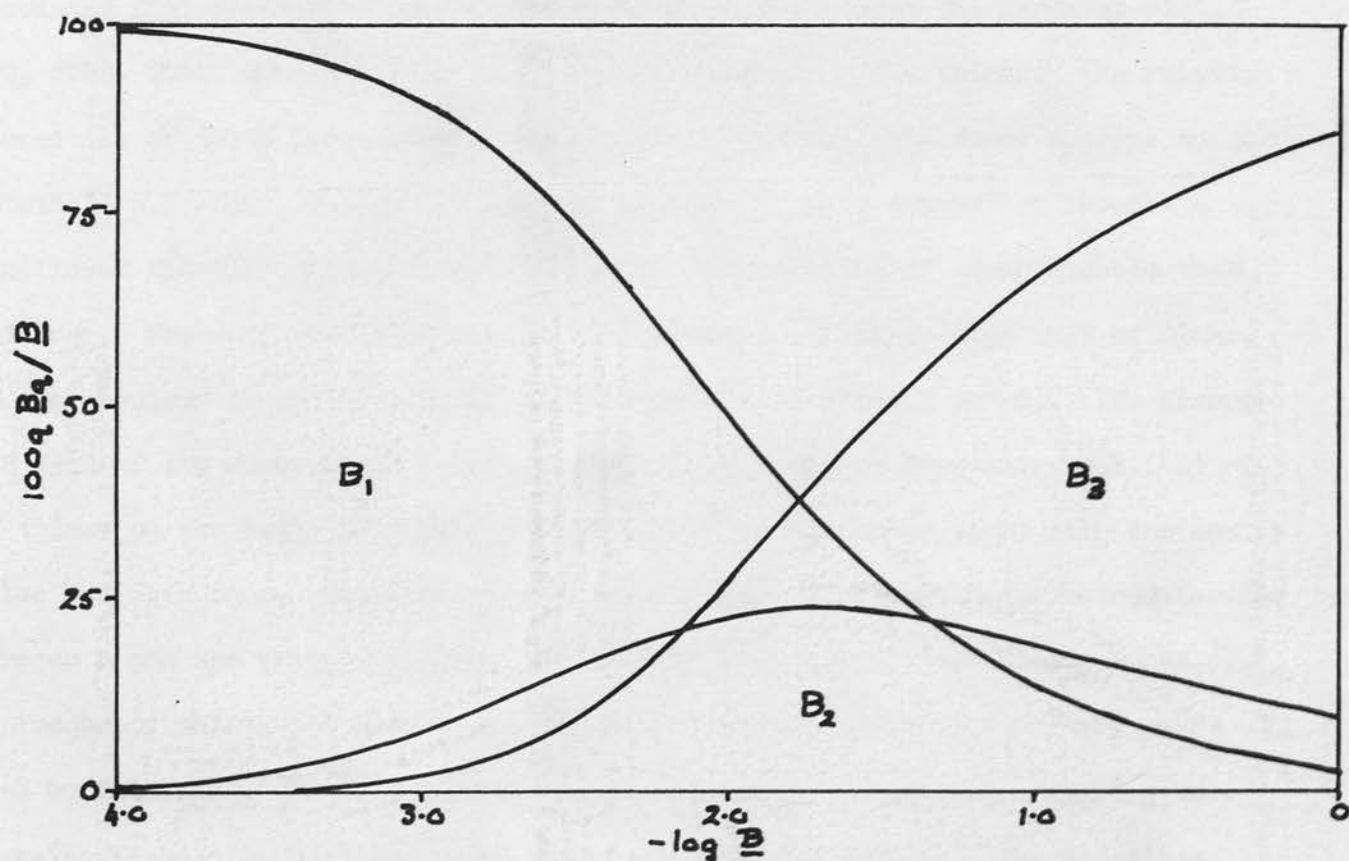
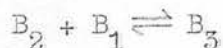


Fig 3. The percentage distributions  $100q Bq/B$  of the pyrazole species in carbon tetrachloride at  $15^\circ\text{C}$ ., plotted as a function of  $\log B$ .

where the pyrazole is approximately 25% dimeric and 37% trimeric. However, the percentages of monomer, which were derived from less precise data in the range  $10^{-2} \leq \underline{B} \leq 1M$  were in good agreement ( $\pm 5\%$ ) with the values calculated using eqn. (3). The values of  $\beta_{20}$  and  $\beta_{30}$  therefore represent the pyrazole system at  $18^\circ C$ . in carbon tetrachloride for total concentrations  $\underline{B} \leq 1M$ .

It is evident from the values of  $\beta_{20}$  and  $\beta_{30}$  that the trimer is much more stable than the dimer. The equilibrium constant for the reaction



is given by  $\beta_{30}/\beta_{20} = 159 \pm 6 \text{ l. mole}^{-1}$ , as compared to the dimerisation constant of  $47.5 \text{ l. mole}^{-1}$ .

An examination of the bonded N-H region, from the viewpoint of the calculated distribution of pyrazole oligomers, suggests that the bands at 5175, 5070, 2995, 2950, 2905 and 2825  $\text{cm.}^{-1}$  may be assigned to the trimer. The relative intensities of these bands remain unchanged as  $\underline{B}$  varies. The dimer appears to contribute a leading edge to the band at 5175  $\text{cm.}^{-1}$ . This absorption becomes a significant shoulder when  $\underline{B} < 10^{-2}M$ , and the concentration of dimer exceeds that of trimer. However, the absorption of the trimer is stronger than that of dimer, and the shoulder is not detectable for  $\underline{B} > 10^{-2}M$  (cf. Figs. 1 and 3). The absorption band of the dimer would be expected to be at a higher frequency than that of the trimer on the basis of Badger's correlation<sup>9</sup> of frequency shift with the energy of the hydrogen bond. Moreover, it has been shown<sup>10</sup> that non-linear intramolecular hydrogen bonds are associated with smaller frequency shifts than linear bonds. The frequency shifts for both dimer and trimer clearly correspond to very short N-H-N bond-lengths, cf.<sup>10</sup>, and indeed, pyrazole in the solid state contains two crystallographically distinct N-H-N bonds, of 2.95 and 2.86  $\text{A.}^5$  The shortness

of these bonds, and also the tendency to self-association in solution, are presumably both due to a markedly unequal charge distribution on the two nitrogen atoms of a pyrazole molecule.

The infrared spectra of pyrazole in other non-associated solvents, e.g. carbon disulphide and chloroform, are qualitatively similar to that in carbon tetrachloride. It is therefore probable that the same equilibria occur.

probably linear.

The infrared spectrum of pyrazole in carbon tetrachloride shows a band at  $1510 \text{ cm}^{-1}$  with a half-width of  $100 \text{ cm}^{-1}$ . This band is assigned to the  $\nu_{15}$  vibration of the pyrazole ring. The band at  $1510 \text{ cm}^{-1}$  is very weak in the spectrum of pyrazole in carbon tetrachloride. This is probably due to the fact that the  $\nu_{15}$  vibration is of low intensity in the free pyrazole molecule.

A weak band at  $1510 \text{ cm}^{-1}$  was observed in the infrared spectrum of pyrazole in carbon disulphide. This band is assigned to the  $\nu_{15}$  vibration of the pyrazole ring. The band at  $1510 \text{ cm}^{-1}$  is very weak in the spectrum of pyrazole in carbon disulphide. This is probably due to the fact that the  $\nu_{15}$  vibration is of low intensity in the free pyrazole molecule.

It was concluded from the above that the  $\nu_{15}$  vibration of the pyrazole ring is of low intensity in the free pyrazole molecule. This is probably due to the fact that the  $\nu_{15}$  vibration is of low intensity in the free pyrazole molecule. It was concluded, however, that the  $\nu_{15}$  vibration of the pyrazole ring is of low intensity in the free pyrazole molecule. This is probably due to the fact that the  $\nu_{15}$  vibration is of low intensity in the free pyrazole molecule.

THE HYDROGEN BONDING OF 3,5-DIMETHYLPYRAZOLE IN CARBON TETRACHLORIDE SOLUTION

A cryoscopic study of 3,5-dimethylpyrazole in benzene has been carried out by White and Kilpatrick.<sup>3</sup> This has given convincing evidence for the existence of a stable trimer, and dubious evidence for an unstable dimer. The authors consider that the trimer is almost certainly cyclic, and the dimer most probably linear.

A preliminary study of dilute solutions of 3,5-dimethylpyrazole in carbon tetrachloride showed a fundamental N-H stretching mode at  $3485 \pm 5 \text{ cm.}^{-1}$  with a half-band width of  $20 \text{ cm.}^{-1}$ , and a broad bonded N-H band extending from  $3400 - 2000 \text{ cm.}^{-1}$ . With increasing total concentration,  $B$ , the intensity of the  $3485 \text{ cm.}^{-1}$  band decreased while that of the bonded N-H band increased. A quantitative study was made of the concentration dependence of the  $3485 \text{ cm.}^{-1}$  band.

Procedure

A stock 0.1000M solution of 3,5-dimethylpyrazole in carbon tetrachloride was prepared by semi-micro weighing. A series of 30 solutions of increasing total concentration  $B$ ,  $10^{-4} \leq B \leq 10^{-2} \text{ M}$ , was prepared by subsequent dilution of the stock solution using an Agla micrometer syringe. Solution temperatures were  $19^{\circ} \pm 1^{\circ} \text{C}$ .

It was impossible to confirm that the intensity of the fundamental N-H stretching of the free monomer conformed to Beer's law as the most dilute solutions ( $B \sim 10^{-4} \text{ M}$ ) that could be studied were still slightly hydrogen bonded ( $\sim 6\%$ ). It was confirmed, however, that the intensity of this band obeyed Lambert's law to within  $\pm 1\%$ , using 4.00, 2.00 and 1.00 cm. cells.

The concentration dependence of the intensity of the 3485 cm.<sup>-1</sup> band was then studied. The value of the apparent molar extinction coefficient of the free monomer was obtained graphically as  $\lim_{B \rightarrow 0} (\log I_0/I)/B$ , where the symbols are the same as for pyrazole. A value of  $\epsilon = 295 \pm 2$  was found, and was used to calculate the free N-H end-group concentrations, e, using eqn. (1). The absorbancies of the 30 solutions and the free N-H end-group concentrations derived therefrom are listed in Table 3.

TABLE 3

Infrared Absorbancies at 3485 cm.<sup>-1</sup> and Free End-Group Concentrations  
of Associated 3,5-dimethylpyrazole in Carbon Tetrachloride  
at 19° ± 1°C

10 <sup>4</sup> B	2.000	3.000	4.000	5.000	6.000	7.000	8.000	9.000	10.00	12.00
log I <sub>0</sub> /I	0.213*	0.306*	0.392*	0.472*	0.548*	0.620*	0.688*	0.749*	0.407†	0.463†
10 <sup>4</sup> e	1.810	2.591	3.322	3.998	4.641	5.248	5.851	6.352	6.857	7.848
10 <sup>4</sup> B	14.00	16.00	18.00	20.00	22.00	24.00	26.00	28.00	30.00	32.00
log I <sub>0</sub> /I	0.513†	0.567†	0.614†	0.654†	0.545	0.369	0.387	0.407	0.422	0.439
10 <sup>4</sup> e	8.711	9.612	10.41	11.09	11.69	12.51	13.12	13.80	14.51	14.88
10 <sup>4</sup> B	36.00	40.00	45.00	50.00	55.00	60.00	70.00	80.00	90.00	100.00
log I <sub>0</sub> /I	0.471	0.498	0.536	0.565	0.597	0.627	0.680	0.730	0.775	0.820
10 <sup>4</sup> e	15.97	16.89	18.18	19.15	20.23	21.25	23.04	24.75	26.26	27.79
* 4.00 cm. cells ) † 2.00 cm. cells ) all other results refer to 1.00 cm. cells.										

Interpretation of the Data

It was found that exactly the same argument held for 3,5-dimethylpyrazole as for pyrazole, and that the experimental data could be represented by the linear equation

$$(\underline{B} - e)/e^2 = 137,150e + 568 \quad (10)$$

with standard deviations in the slope and intercept of  $\pm 2,150$  and  $\pm 3.2$  respectively, found by an unweighted least squares treatment. Hence,  $e$  is a true measure of the free monomer concentration,  $b$ , (see Table 2), and the system consists of free monomer, cyclic dimer and cyclic trimer species only. Values of the two association constants derived from eqn. (10) are

$$\beta_{20} = 284 \pm 1.6 \text{ l. mole}^{-1} \quad \text{and} \quad \beta_{30} = 45,700 \pm 720 \text{ l.}^2 \text{ mole}^{-2}.$$

The values of the association constants were checked by the curve-fitting method as for pyrazole. The experimental curve of  $\log \{(\underline{B} - b)/b^2\}$  against  $\log b$  and the normalised curve of  $\log (1 + \frac{b}{\underline{m}})$  against  $\log \frac{b}{\underline{m}}$  were superimposed, and, in the position of best fit (see Fig. 4), the equations

$$\log (1 + \frac{b}{\underline{m}}) = \log \{(\underline{B} - b)/b^2\} - \log 2\beta_{20} \quad (7)$$

and

$$\log \frac{b}{\underline{m}} = \log b + \log (3\beta_{30}/2\beta_{20}) \quad (8)$$

were solved for  $\beta_{20}$  and  $\beta_{30}$ . By this method, values of

$$\beta_{20} = 284 \pm 3.0 \text{ l. mole}^{-1} \quad \text{and} \quad \beta_{30} = 46,200 \pm 1600 \text{ l.}^2 \text{ mole}^{-2}$$

were obtained, the errors being estimated from the permissible relative displacements of the experimental and normalised curves, parallel to the coordinate axes. The agreement between the two sets of results is excellent.

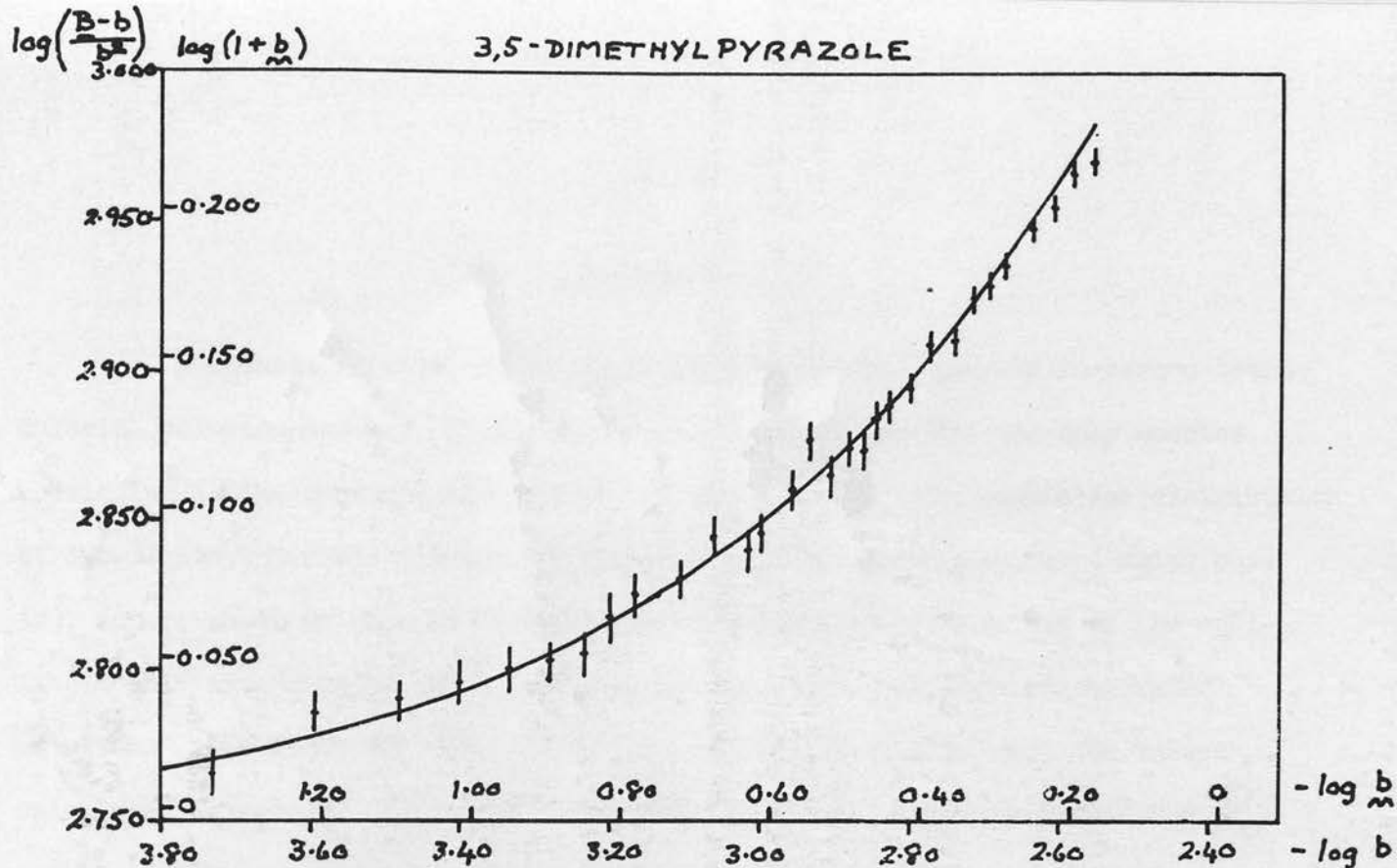


Fig. 4. The experimental data  $\log\left[\frac{(B-b)}{b^2}\right]: \log b$  superimposed in the position of best fit on the normalised curve  $\log(1+\frac{b}{m}): \log b$ .

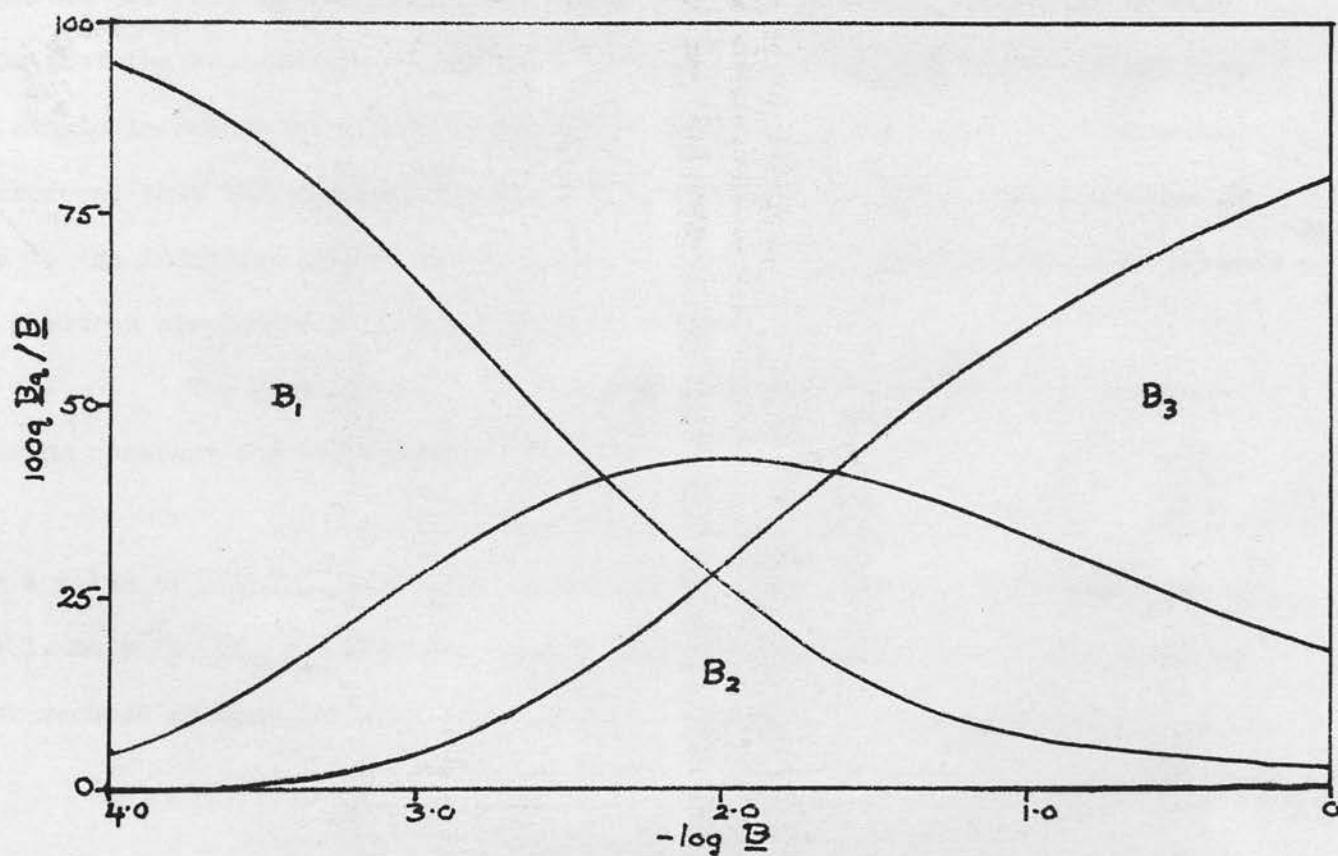


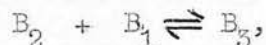
Fig. 5. The percentage distributions  $100q \frac{B_q}{B}$  of the 3,5-dimethylpyrazole species in carbon tetrachloride at 19°C., plotted as a function of  $\log B$ .

### Discussion

These results confirm that for 3,5-dimethylpyrazole in carbon tetrachloride solution, monomer, cyclic dimer and cyclic trimer are the only species coexisting in the concentration range  $10^{-4} \leq \underline{B} \leq 10^{-2} \text{M}$ . The percentage distribution of 3,5-dimethylpyrazole between the three species has been calculated using eqn. (3), and is shown in Fig. 5. The precise infrared data used to deduce the equilibria only extend up to  $10^{-2} \text{M}$ , but less precise data from more concentrated solutions ( $10^{-2} \leq \underline{B} \leq 1 \text{M}$ ) were in substantial agreement ( $\pm 5\%$ ) with the values calculated using eqn. (3). It is concluded, therefore, that the values for  $\beta_{20}$  and  $\beta_{30}$  fully describe the 3,5-dimethylpyrazole system in carbon tetrachloride at  $19^\circ \text{C}$ . for total concentrations,  $\underline{B} \leq 1 \text{M}$ .

As compared with pyrazole, the values of  $\beta_{20}$  and  $\beta_{30}$  for 3,5-dimethylpyrazole are both approximately six times as great. Accurate molecular models show that the replacement of two hydrogen atoms by two methyl groups should have no steric influence on either cyclic dimer or trimer formation. It is proposed, therefore, that the enhanced stability of the cyclic dimethylpyrazole species is due to the inductive effect of the methyl groups, which stabilise the N-H...N bonds by electron displacement into the pyrazole rings.

The ratio  $\beta_{30}/\beta_{20}$  for 3,5-dimethylpyrazole, which gives the equilibrium constant for the reaction



has a value of  $162 \pm 6 \text{ l. mole}^{-1}$ , as compared to the dimerisation constant of  $284 \text{ l. mole}^{-1}$ . The tendency for cyclic trimer to be formed from cyclic dimer is thus reduced as compared with the case of pyrazole, where the corresponding values

are  $\beta_{30}/\beta_{20} = 159 \text{ l. mole}^{-1}$  and  $\beta_{20} = 47.5 \text{ l. mole}^{-1}$ . It is doubtful that the methyl groups have any steric effect on the stability of the trimer. It is therefore probable that the difference is due to the methyl groups increasing the difficulty of the monomer and dimer attaining the correct spatial configuration prior to combination to form the trimer.

Since the infrared spectra of 3,5-dimethylpyrazole in other non-associated solvents are quantitatively similar to that in carbon tetrachloride, it is probable that the same equilibria occur.

#### Procedure

A stock 0.100M solution of 3,5-dimethylpyrazole in carbon tetrachloride was prepared by exact micro weighing. A series of 24 solutions of increasing total concentration  $3 \times 10^{-3} \leq C \leq 1.4 \times 10^{-2}$ , was prepared by subsequent dilution of the stock solution using an agitator apparatus. Solution temperatures were  $21 \pm 0.1^\circ\text{C}$ .

Confirmation that the intensity of the fundamental 851 band obeyed Beer's law was not obtainable since the most dilute solutions ( $3 \times 10^{-3} \text{ M}$ ) that could be studied still exhibited some hydrogen bonding ( $\nu_{\text{OH}}$ ). The intensity of the band was found to conform to Lambert's law to within  $\pm 5\%$  using 4.00, 2.00 and 1.00 cm. cells.

The concentration dependence of the intensity of the 850 cm.<sup>-1</sup> band was then studied. The values of the apparent molar extinction coefficient of the free species was obtained graphically as  $\log I_0/I$  vs.  $C$ ; a value of  $\epsilon = 320 \pm 1$  was found, and used to calculate the free monomer concentrations,  $m_1$ , for all the solutions using eqn. (1). The characteristics of the 24 solutions,

THE HYDROGEN BONDING OF 3,5-DIETHYLPYRAZOLE IN CARBON TETRACHLORIDE SOLUTION

Solutions of 3,5-diethylpyrazole in carbon tetrachloride in the concentration range  $10^{-5}$  -  $1M$  were found to exhibit a fundamental N-H stretching mode at  $3480 \pm 5 \text{ cm.}^{-1}$  with a half-band width of  $20 \text{ cm.}^{-1}$ , in equilibrium with a broad, bonded N-H band extending from  $3400 - 2000 \text{ cm.}^{-1}$ . A quantitative study of the concentration dependence of the  $3480 \text{ cm.}^{-1}$  band was made to determine the nature of the 3,5-diethylpyrazole oligomers in carbon tetrachloride solution.

Procedure

A stock  $0.1000M$  solution of 3,5-diethylpyrazole in carbon tetrachloride was prepared by semi-micro weighing. A series of 24 solutions of increasing total concentration  $B$ ,  $10^{-4} \leq B \leq 8 \times 10^{-3}M$ , was prepared by subsequent dilution of the stock solution using an Agla micrometer syringe. Solution temperatures were  $21^{\circ} \pm 1^{\circ}C$ .

Confirmation that the intensity of the fundamental N-H band obeyed Beer's law was not obtainable since the most dilute solutions ( $B \sim 10^{-4}M$ ) that could be studied still exhibited some hydrogen bonding ( $\sim 3\%$ ). The intensity of the band was found to conform to Lambert's law to within  $\pm 1\%$  using 4.00, 2.00 and 1.00 cm. cells.

The concentration dependence of the intensity of the  $3480 \text{ cm.}^{-1}$  band was then studied. The value of the apparent molar extinction coefficient of the free monomer was obtained graphically as  $\lim_{B \rightarrow 0} (\log I_0/I)/B$ : a value of  $\xi = 225 \pm 1$  was found, and used to calculate the free N-H end-group concentrations,  $e$ , for all the solutions using eqn. (1). The absorbancies of the 24 solutions,

and the free end-group concentrations calculated therefrom, are collected in Table 4.

TABLE 4

Infrared Absorbancies at 3480 cm.<sup>-1</sup> and Free End-Group Concentrations of Associated 3,5-diethylpyrazole in Carbon Tetrachloride at 21° ± 1°C

10 <sup>4</sup> <u>B</u>	1.000	2.000	3.000	4.000	5.000	6.000	7.000	8.000
log I <sub>o</sub> /I	0.088*	0.172*	0.254*	0.332*	0.408*	0.481*	0.552*	0.621*
10 <sup>4</sup> e	0.978	1.916	2.821	3.688	4.528	5.343	6.129	6.901
10 <sup>4</sup> <u>B</u>	9.000	10.00	12.00	14.00	16.00	18.00	20.00	25.00
log I <sub>o</sub> /I	0.687*	0.751*	0.439†	0.498†	0.553†	0.608†	0.662†	0.390
10 <sup>4</sup> e	7.633	8.337	9.761	11.07	12.28	13.51	14.71	17.34
10 <sup>4</sup> <u>B</u>	30.00	35.00	40.00	45.00	50.00	60.00	70.00	80.00
log I <sub>o</sub> /I	0.447	0.501	0.547	0.595	0.640	0.720	0.791	0.856
10 <sup>4</sup> e	19.86	22.26	24.31	26.44	28.44	32.00	35.16	38.05
* 4.00 cm. cells ) † 2.00 cm. cells ) all other results refer to 1.00 cm. cells.								

Interpretation of the Data

As in the cases of pyrazole and 3,5-dimethylpyrazole, it was found that the experimental data could be represented by a linear equation. The equation

$$(\underline{B} - e)/e^2 = 18,500e + 219 \quad (11)$$

was derived from the data, with standard deviations in the slope and intercept of  $\pm 500$  and  $\pm 3.0$  respectively, found by an unweighted least squares treatment. Thus  $e$  is a true representation of the free monomer concentration,  $b$ , (see Table 2), and the system consists of monomer, cyclic dimer and cyclic trimer species only, with equilibrium constants given by

$$\beta_{20} = 110 \pm 1.5 \text{ l. mole}^{-1} \quad \text{and} \quad \beta_{30} = 6,100 \pm 170 \text{ l.}^2 \text{ mole}^{-2}.$$

The curve fitting method was used to check the values of the association constants. The same mathematical argument applies as in the cases of pyrazole and 3,5-dimethylpyrazole. The experimental curve of  $\log \left\{ \frac{B - b}{b^2} \right\}$  against  $\log b$  and the normalised curve of  $\log (1 + \frac{b}{\beta_{20}})$  against  $\log \frac{b}{\beta_{20}}$  were superimposed, and, in the position of best fit (see Fig. 6), eqns. (7) and (8) were solved for  $\beta_{20}$  and  $\beta_{30}$ , giving

$$\beta_{20} = 110 \pm 1.0 \text{ l. mole}^{-1} \quad \text{and} \quad \beta_{30} = 6,010 \pm 220 \text{ l.}^2 \text{ mole}^{-2},$$

in good agreement with the previous values.

### Discussion

The percentage distribution of 3,5-diethylpyrazole between monomer, cyclic dimer and cyclic trimer has been calculated using eqn. (3), and is shown in Fig. 7. In the range  $8 \times 10^{-5} \leq B \leq 1M$ , no precise measurements were taken, but it was observed that the absorbancies of the  $5480 \text{ cm.}^{-1}$  band were in substantial agreement with those predicted from Fig. 7. The values for  $\beta_{20}$  and  $\beta_{30}$  are therefore concluded to fully describe the 3,5-diethylpyrazole system in carbon tetrachloride at  $21^\circ\text{C}$ . for total concentrations,  $B \leq 1M$ .

Molecular models of the bonded species of 3,5-diethylpyrazole show that the ethyl groups cause a slight hindrance to cyclic dimer formation and a

3,5-DIETHYLPYRAZOLE

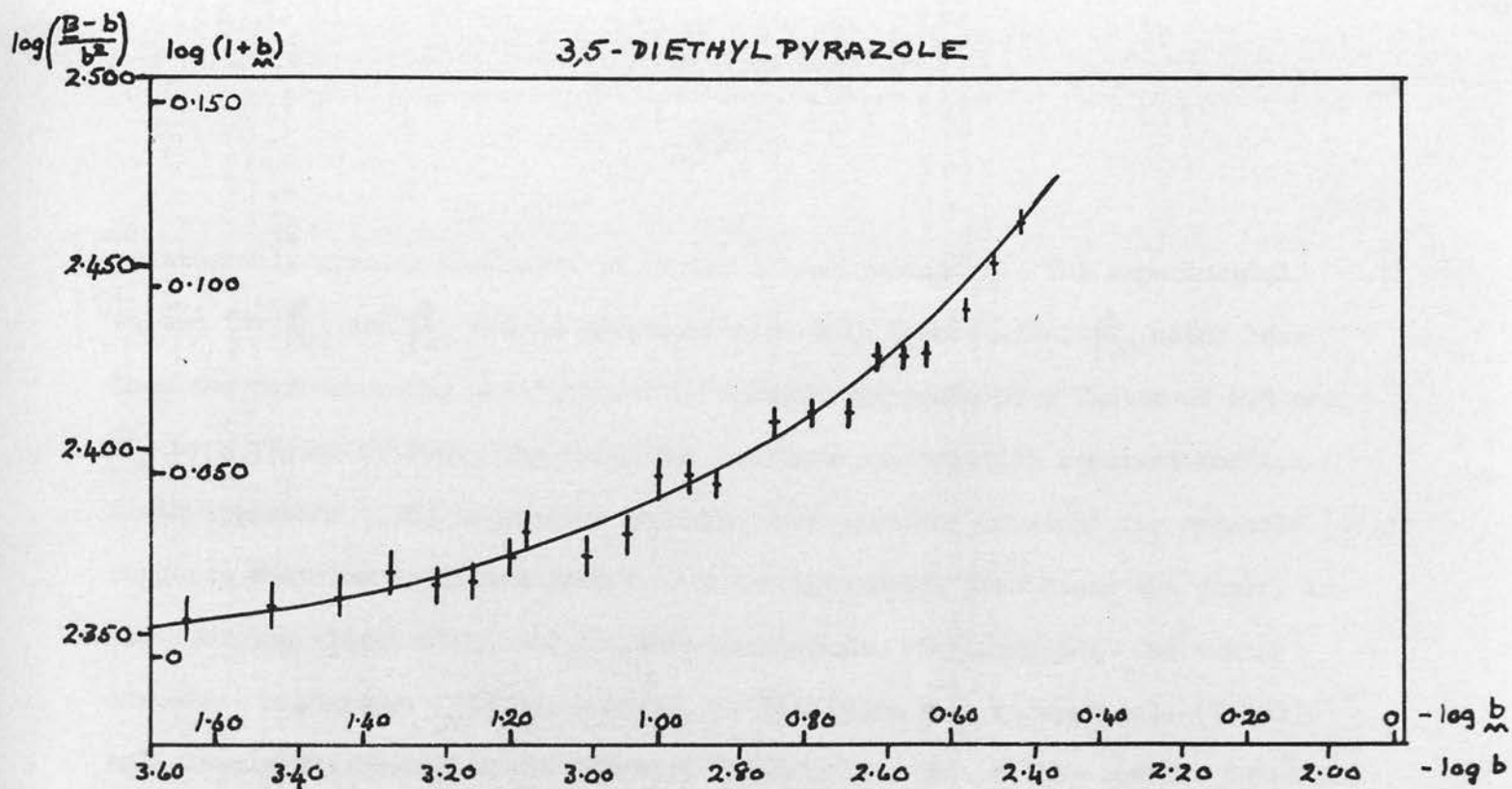


Fig. 6. The experimental data  $\log\left[\frac{(B-b)}{b^2}\right] : \log b$  superimposed in the position of best fit on the normalised curve  $\log(1+b) : \log b$ .

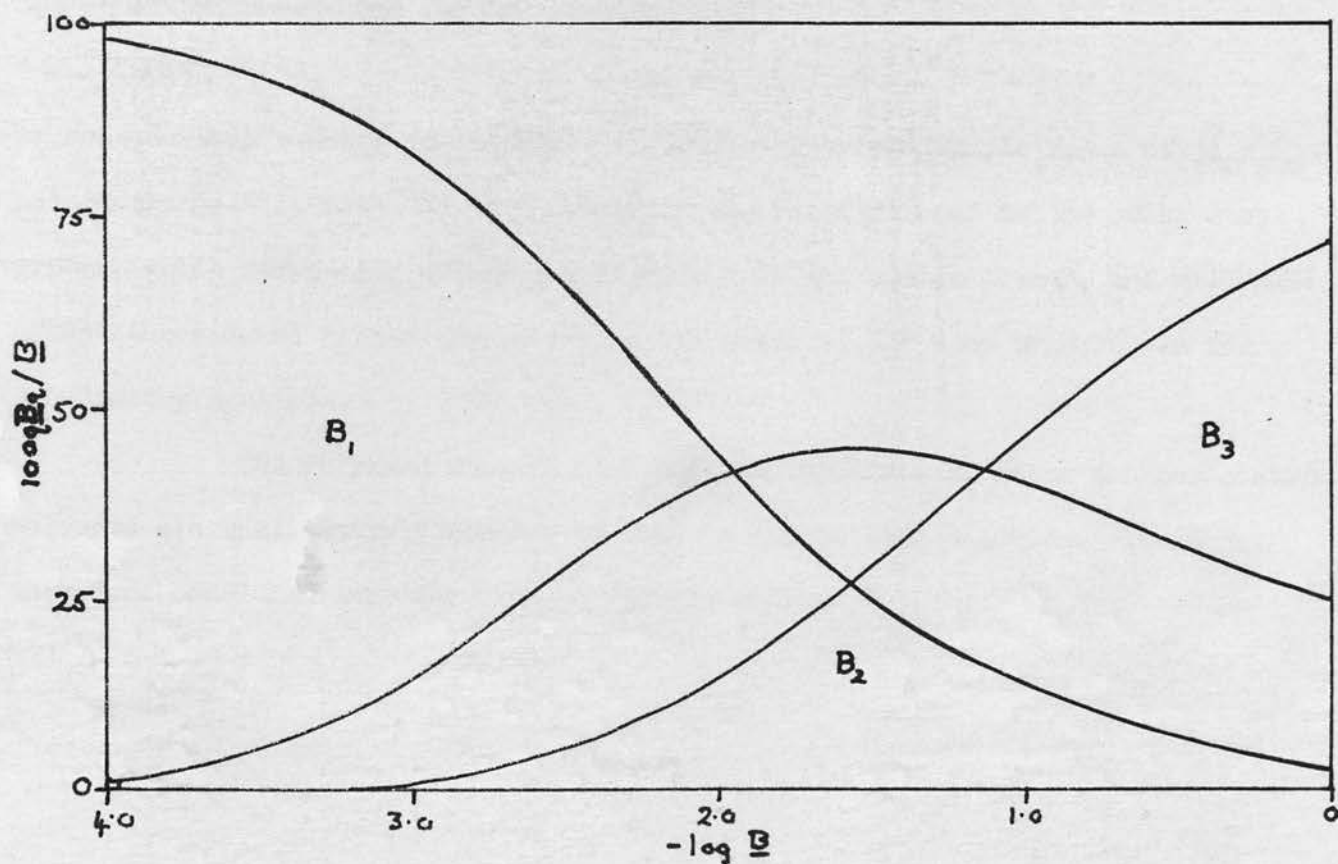
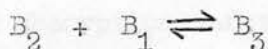


Fig. 7. The percentage distributions  $100q_{B_i}/B$  of the 3,5-diethylpyrazole species in carbon tetrachloride at 21°C., plotted as a function of  $\log B$ .

considerably greater hindrance to cyclic trimer formation. The experimental values for  $\beta_{20}$  and  $\beta_{30}$  are in agreement with this observation,  $\beta_{20}$  being less than the corresponding constant for 3,5-dimethylpyrazole by a factor of 2.6 and  $\beta_{30}$  by a factor of 7.6. The fact that the dimer association constant for 3,5-diethylpyrazole (110) is greater than the corresponding constant for pyrazole (47.5) suggests that the inductive effect of the ethyl groups stabilises the dimer, in spite of the slight steric interaction between the ethyl groups. The trimer association constant (6,000), however, is less than that for pyrazole (7,500), and clearly the steric interactions of the ethyl groups in this species completely overcome their stabilising effect.

As compared with the cases of pyrazole and 3,5-dimethylpyrazole, the equilibrium constant for the reaction



is considerably reduced in the case of 3,5-diethylpyrazole, the value of  $\beta_{30}/\beta_{20}$  being only 55.5 l. mole<sup>-1</sup>. This reduction can be attributed to the bulky ethyl groups, which sterically affect the stability of the cyclic trimer, and will also affect the ease of trimer formation, on the basis of the same argument as for 3,5-dimethylpyrazole.

The infrared spectra of 3,5-diethylpyrazole in other non-associated solvents are qualitatively similar to that in carbon tetrachloride. It is therefore concluded that the same equilibria obtain.

THE HYDROGEN BONDING OF 3,5-DIPHENYLPYRAZOLE IN CARBON TETRACHLORIDE SOLUTION

3,5-diphenylpyrazole is relatively insoluble in carbon tetrachloride as compared with pyrazole, 3,5-dimethylpyrazole and 3,5-diethylpyrazole, all of which can form 1M solutions. A saturated solution of 3,5-diphenylpyrazole has a total concentration,  $\underline{B} = 2 \times 10^{-3} \text{M}$ .

A preliminary study of the infrared spectra of solutions of 3,5-diphenylpyrazole in carbon tetrachloride in the concentration range  $10^{-4} \leq \underline{B} \leq 2 \times 10^{-3} \text{M}$  showed a fundamental N-H stretching mode at  $3475 \pm 5 \text{ cm.}^{-1}$  with a half-band width of  $20 \text{ cm.}^{-1}$ , in equilibrium with a broader band at  $3255 \pm 10 \text{ cm.}^{-1}$  and a broad, bonded N-H band with fine structure in the region  $3100 - 2700 \text{ cm.}^{-1}$ . On the basis of a comparison of the spectra of 3,5-diphenylpyrazole with those of the previous three compounds discussed, the  $3255 \text{ cm.}^{-1}$  band was attributed to the N-H absorption of a cyclic dimer. The N-H absorptions of the cyclic dimers of pyrazole, 3,5-dimethylpyrazole and 3,5-diethylpyrazole were found to absorb at  $3240 \pm 10 \text{ cm.}^{-1}$  (see Fig. 1),  $3240 \pm 10 \text{ cm.}^{-1}$ , and  $3250 \pm 10 \text{ cm.}^{-1}$  respectively. On the other hand, the N-H absorption of the linear dimer of imidazole in carbon tetrachloride was found to absorb at  $3125 \pm 10 \text{ cm.}^{-1}$ . This lower frequency was expected, since linear hydrogen bonds are generally associated with larger frequency shifts than non-linear, strained hydrogen bonds. It was therefore concluded that the  $3255 \text{ cm.}^{-1}$  band of 3,5-diphenylpyrazole was due to the N-H absorption of a cyclic dimer.

A quantitative study of the concentration dependence of the intensity of the  $3475 \text{ cm.}^{-1}$  band was made to determine the nature of the 3,5-diphenylpyrazole oligomers in carbon tetrachloride solution.

### Procedure

A stock  $2.000 \times 10^{-5} M$  solution of 3,5-diphenylpyrazole in carbon tetrachloride was prepared by semi-micro weighing. Solutions in the concentration range  $10^{-4} \leq \underline{B} \leq 10^{-5} M$  were prepared by accurate dilution of this stock solution using an Agla micrometer syringe. More concentrated solutions,  $10^{-5} \leq \underline{B} \leq 2 \times 10^{-5} M$ , were prepared by direct weighing. A series of 14 solutions were prepared. Solution temperatures were  $21^{\circ} \pm 1^{\circ} C$ .

Since the most dilute solutions ( $\underline{B} \sim 10^{-4} M$ ) that could be studied were slightly hydrogen bonded ( $\sim 5\%$ ) no confirmation that the intensity of the  $3475 \text{ cm.}^{-1}$  band obeyed Beer's law was obtained. It was shown, however, that the intensity of the band obeyed Lambert's law to within  $\pm 1\%$ , using 4.00 and 2.00 cm. cells.

The concentration dependence of the intensity of the  $3475 \text{ cm.}^{-1}$  band was then studied. The value of the apparent molar extinction coefficient of the free monomer was obtained graphically as  $\lim_{\underline{B} \rightarrow 0} (\log I_0/I)/\underline{B}l$ : only a short extrapolation was necessary to give the accurate value  $\epsilon = 258 \pm 1$ . This was used to calculate the free N-H end-group concentrations,  $e$ , for all the solutions using eqn. (1). Details of the 14 solutions used ( $10^{-4} \leq \underline{B} \leq 2 \times 10^{-5} M$ ) and the calculated end-group concentrations are collected in Table 5.

### Interpretation of the Data

It was found that the experimental data did not conform to a linear equation of the type

$$(\underline{B} - e)/e^2 = 2\beta_{20} + 3\beta_{50}e.$$

TABLE 5

Infrared Absorbancies at  $3475 \text{ cm.}^{-1}$  of Associated 3,5-diphenylpyrazole in Carbon Tetrachloride at  $21^\circ \pm 1^\circ \text{C.}$ , and Concentration Variables derived therefrom

$10^4 \underline{B}$	$\log I_o/I$	$10^4 \underline{e}$	$10^4 \underline{S}$	$10^4 \underline{b}$	$10^4 \underline{B}$	$\log I_o/I$	$10^4 \underline{e}$	$10^4 \underline{S}$	$10^4 \underline{b}$
1.000	0.1000	0.969	--	--	8.000	0.636	6.171	6.700	5.866
2.000	0.1936	1.880	1.934	1.870	9.000	0.695	6.740	7.359	6.340
3.000	0.281	2.721	2.833	2.695	10.00	0.749	7.259	7.938	6.738
4.000	0.363	3.519	3.706	3.466	12.00	0.421*	8.156	9.004	7.427
5.000	0.438	4.245	4.512	4.151	14.00	0.464*	8.993	9.977	8.007
6.000	0.511	4.952	5.505	4.797	16.00	0.503*	9.738	10.84	8.484
7.000	0.576	5.580	6.023	5.359	18.00	0.538*	10.42	11.63	8.888

\* 2.00 cm. cells; all other results refer to 4.00 cm. cells.

The system, therefore, could not be described in terms of monomer, cyclic dimer and cyclic trimer only, but clearly contained higher oligomers. The preliminary infrared studies outlined above gave convincing evidence for the presence of a cyclic dimer, and molecular models showed that this structure is capable of existence with only a slight degree of interaction between the benzene rings. The models showed, however, that a cyclic trimer is sterically incapable of formation due to the interactions of the benzene rings, although a linear trimer is almost completely unhindered and should be capable of existence. It was also seen that higher linear oligomers should be capable of formation. It was therefore assumed that the 3,5-diphenylpyrazole system existed as an equilibrium between monomer, cyclic dimer and higher linear oligomers. On the reasonable assumption that the

values of the extinction coefficients of all linear oligomers are equal, eqn. (1) may be rewritten for the 5,5-diphenylpyrazole system as

$$(1/\mathcal{E}_1) \log I_0/I = e = \underline{B}_1 + \sum_1^Q \underline{B}_q \quad (12)$$

where  $\mathcal{E}_1$  is the experimentally measured molar extinction coefficient of the free monomer, and  $Q$  is the maximum value of  $q$  in the system.

For any self-associated system, the total concentration,  $\underline{B}$ , is related to the free monomer concentration,  $b$ , by the equation

$$\underline{B} = \sum_1^Q q \underline{B}_q = \sum_1^Q q \beta_{q0} b^q \quad (13)$$

where the self-association constants,  $\beta_{q0}$ , are defined by

$$\beta_{q0} = \underline{B}_q / b^q. \quad (14)$$

Similarly, for the sum of the concentrations of all oligomers,  $\underline{S}$ ,

$$\underline{S} = \sum_1^Q \underline{B}_q = \sum_1^Q \beta_{q0} b^q. \quad (15)$$

$\underline{B}$ ,  $\underline{S}$  and  $b$  are simply inter-related by Bjerrum's integral<sup>11</sup>

$$\log b/b_1 = (1/2.303) \int_{\underline{S}_1}^{\underline{S}} (1/\underline{B}) d\underline{S} \quad (16)$$

Hence, values of  $b$  may be calculated from the experimental data ( $1/\underline{B}$ ,  $\underline{S}$ ) without making any assumptions about the equilibria, provided that a value  $\underline{S}_1$ , of  $\underline{S}$ ,

corresponding to a known value  $b_1$  of the monomer concentration can be selected.

A point ( $\underline{S}_1$ ,  $b_1$ ) may be found by a method suggested by Rossotti and Rossotti.<sup>12</sup>

In sufficiently dilute solutions, where the dimer is the sole oligomer, eqns.

(13), (14) and (15) may be combined to give

$$(\underline{B} - \underline{S}) = \beta_{20} b^2 = \beta_{20} (2\underline{S} - \underline{B}).$$

Hence

$$\log (\underline{B} - \underline{S}) = \log \beta_{20} + 2 \log (2\underline{S} - \underline{B}), \quad (17)$$

and a plot of  $\log (\underline{B} - \underline{S})$  against  $\log (2\underline{S} - \underline{B})$  tends to a straight line of slope

2 as  $\underline{S} \rightarrow \underline{B}$ . A point ( $\underline{B}_1$ ,  $\underline{S}_1$ ) is found by solution of eqn. (17) and the corres-

ponding value of  $b_1$  by substitution into the equation

$$b_1 = (2\underline{S}_1 - \underline{B}_1).$$

However, the experimental data for 3,5-diphenylpyrazole gave values for the free end-group concentrations,  $e$ , by eqn. (12), and it was necessary to calculate the corresponding values of  $\underline{S}$ , before Bjerrum's integral (16) could be used to inter-relate  $\underline{B}$ ,  $\underline{S}$ , and  $b$ . This was carried out by a method of successive approximations using the integral (16).

In the first instance a point ( $e_1, b_1$ ) was found from the experimental results, and  $e$  was substituted for  $\underline{S}$  in the integral. Using the values of  $b^I$  found by resultant graphical integration, a plot of  $(\underline{B} - b^I)/2(b^I)^2$  against  $b^I$  was used to give a value for  $\beta_{20}^I$  as the intercept on the ordinate axis. The experimental values of  $e$  were then corrected to  $\underline{S}^I$  using the relation

$$\underline{S}^I = e + \beta_{20}^I (b^I)^2$$

which can be derived by a comparison of eqns. (12) and (15). Graphical integration was repeated using  $\underline{S}^I$  in place of  $e$ . A second value for the dimer association constant,  $\beta_{20}^{II}$ , was found as before, and using the above relationship, values of  $\underline{S}^{II}$  were calculated from the corresponding values of  $e$ . A further five complete cycles were performed before the following conditions were satisfied:

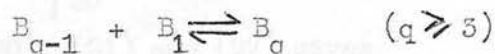
- a)  $\underline{S}^{VI} = e + \beta_{20}^V (b^V)^2 = \underline{S}^V$ , and further graphical integration gave identical values for  $\underline{S}$ ,  $b$  and  $\beta_{20}$ ;
- b) plots of  $(\underline{B} - b^V)/2(b^V)^2$  and  $(\underline{S} - b^V)/(b^V)^2$  against  $b^V$  gave the same intercept on the ordinate axis; and
- c) a plot of  $(e - b^V)/(b^V)^2$  against  $b^V$  passed through the origin.

It was considered that the final values of  $\underline{S}$  and  $b$  were therefore the true experimental values for the 3,5-diphenylpyrazole system. These final values are included in Table 5.

Calculation of the Stability Constants.- Two methods were used, and these are individually reported.

1) Curve fitting. Methods, devised by Rossotti and Rossotti,<sup>13</sup> were used. For a system which exists in stepwise equilibrium, four two-parameter models, calculated on simple hypotheses, may be considered.

Hypothesis I. If the stepwise association constants for the reactions



are all assumed to be equal and to have a value  $K$ , then

$$\beta_{q0} = \beta_{20} K^{q-2} \quad (q \geq 2). \quad (18)$$

Then, combining eqns. (15) and (18),

$$T = (\underline{B} - b)/b = \sum_2^{\infty} q \beta_{20} K^{q-2} b^{q-1} \quad (19)$$

considering an infinite system. Defining normalised variables  $\underline{T}$  and  $\underline{b}$  by

$$\underline{T} = TK/\beta_{20} \quad (20)$$

and

$$\underline{b} = Kb \quad (21)$$

and combining eqns. (19), (20) and (21) gives

$$\underline{T} = \underline{b}(2 - \underline{b})/(1 - \underline{b})^2. \quad (22)$$

Similarly, from eqns. (15) and (18),

$$\theta = (\underline{S} - b)/b = \sum_2^{\infty} \beta_{20} K^{q-2} b^{q-1} \quad (23)$$

considering an infinite system. Defining a further normalised variable  $\underline{\theta}$  by

$$\underline{\theta} = K/\beta_{20} \quad (24)$$

and combining eqns. (21), (23) and (24) gives

$$\underline{\theta} = \underline{b}/(1 - \underline{b}). \quad (25)$$

The normalised equations (22) and (25) are valid provided that  $\underline{b} < 1$ .

Hypothesis II. If the first few stepwise associations occur less readily than the rest, we may set

$$K_q = (q - 2)K/(q - 1) \quad (q \geq 3). \quad (26)$$

Hence  $K_q \rightarrow K$  as  $q \rightarrow \infty$ , and

$$\beta_{q0} = \beta_{20} K^{q-2}/(q - 1) \quad (q \geq 2). \quad (27)$$

Combining eqns. (19), (20), (21) and (27) gives

$$\bar{T} = \sum_{m=2}^{\infty} q b^{q-1}/(q - 1) = \frac{b}{1 - b} - \ln(1 - b). \quad (28)$$

Similarly, combining eqns. (21), (25), (24) and (27) gives

$$\bar{\theta} = \sum_{m=2}^{\infty} b^{q-1}/(q - 1) = -\ln(1 - b). \quad (29)$$

Equations (28) and (29) are valid provided  $b < 1$ .

Hypothesis III. Assuming that each addition to the growing polymer chain becomes progressively more difficult, we may set

$$K_q = K/(q - 1) \quad (q \geq 3). \quad (30)$$

Hence  $K_q \rightarrow 0$  as  $q \rightarrow \infty$ , and

$$\beta_{q0} = \beta_{20} K^{q-2}/(q - 1)! \quad (q \geq 2). \quad (31)$$

The normalised equations for  $\bar{T}$  and  $\bar{\theta}$ , defined by eqns. (20) and (24), then become

$$\bar{T} = \sum_{m=2}^{\infty} q b^{q-1}/(q - 1)! = \exp^b (1 + \frac{b}{m}) - 1 \quad (32)$$

and

$$\bar{\theta} = \sum_{m=2}^{\infty} b^{q-1}/(q - 1)! = \exp^b - 1 \quad (33)$$

provided  $b < 1$ .

Hypothesis IV. Finally, assuming that the first few stepwise associations occur more readily than the rest, we may set

$$K_q = (q - 1)K/(q - 2) \quad (q \geq 3). \quad (34)$$

Hence  $K_q \rightarrow K$  as  $q \rightarrow \infty$ , and

$$\beta_{q0} = \beta_{20}(q-1)K^{q-2} \quad (q \geq 2). \quad (35)$$

The normalised equations for  $\frac{T}{m}$  and  $\frac{\theta}{m}$  then become

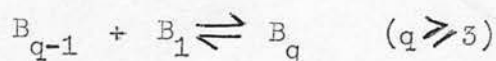
$$\frac{T}{m} = \sum_2^q q(q-1) \frac{b}{m}^{q-1} = \frac{2b}{m} / (1 - \frac{b}{m})^3 \quad (36)$$

and

$$\frac{\theta}{m} = \sum_2^q (q-1) \frac{b}{m}^{q-1} = \frac{b}{m} / (1 - \frac{b}{m})^2 \quad (37)$$

again provided  $\frac{b}{m} < 1$ .

For the 3,5-diphenylpyrazole system, the experimental data was plotted in the form  $\log T$  ( $\log b$ ) and  $\log \theta$  ( $\log b$ ), where  $T$  and  $\theta$  are defined by eqns. (19) and (23). These functions were compared with the various pairs of normalised curves  $\log \frac{T}{m}$  ( $\log \frac{b}{m}$ ) and  $\log \frac{\theta}{m}$  ( $\log \frac{b}{m}$ ) calculated for the above hypotheses. It was found that the experimental curves were of the same shape as pairs of normalised curves calculated on the assumptions made in Hypotheses I, III and IV. It may therefore be said that the 3,5-diphenylpyrazole system in carbon tetrachloride is most simply described on the assumptions made in Hypothesis I, and that the stepwise association constants for the reactions



all have the same value  $K$ . From the positions of best fit of the experimental and normalised curves for Hypothesis I (see Fig. 8), it was found that

$$\log \beta_{20} = 2.19 \pm 0.03$$

and

$$\log K = 2.82 \pm 0.01$$

Hence, for the 3,5-diphenylpyrazole system in carbon tetrachloride at  $21^\circ \pm 1^\circ\text{C}$ ., the association constants are given by

$$\beta_{20} = 155 \pm 10 \text{ l. mole}^{-1} \quad \text{and} \quad K = 661 \pm 6 \text{ l. mole}^{-1}.$$

Values for the first few self-association constants of the

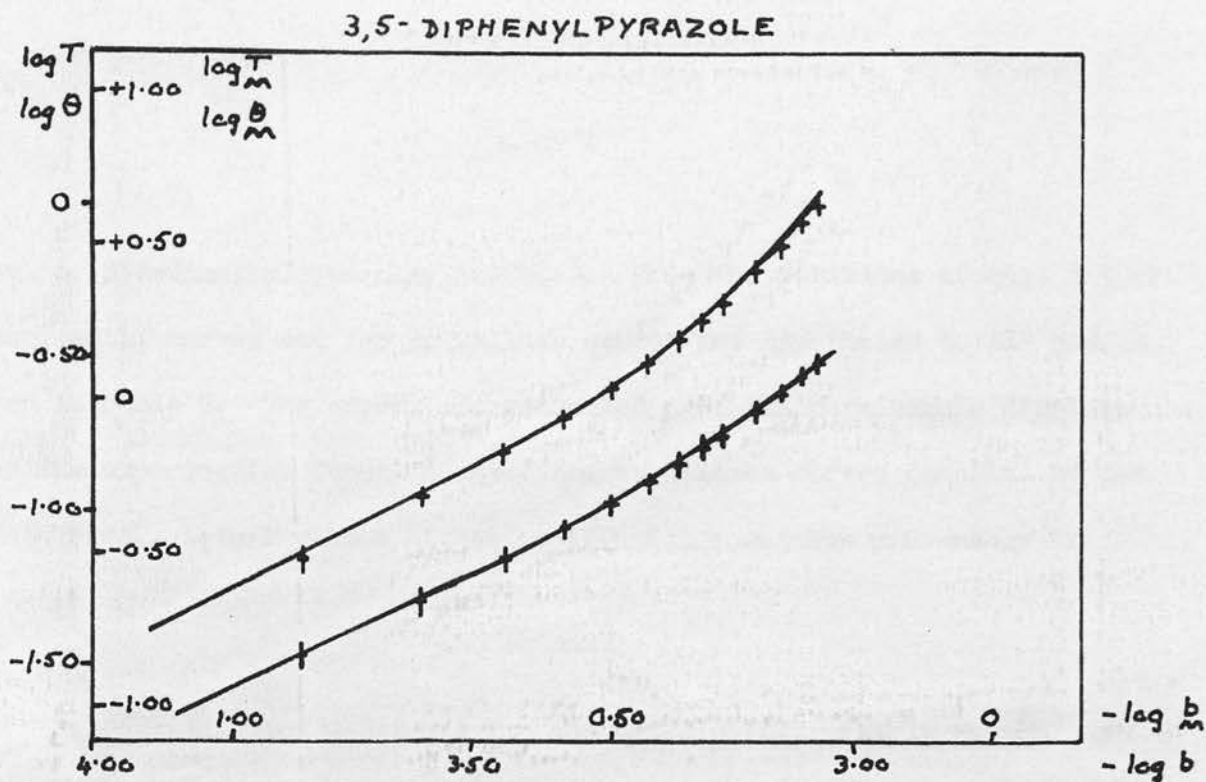


Fig. 8. The experimental data  $\log T(\log b)$  and  $\log \theta(\log b)$  superimposed in the position of best fit on normalised curves calculated using eqns. (22) and (25).

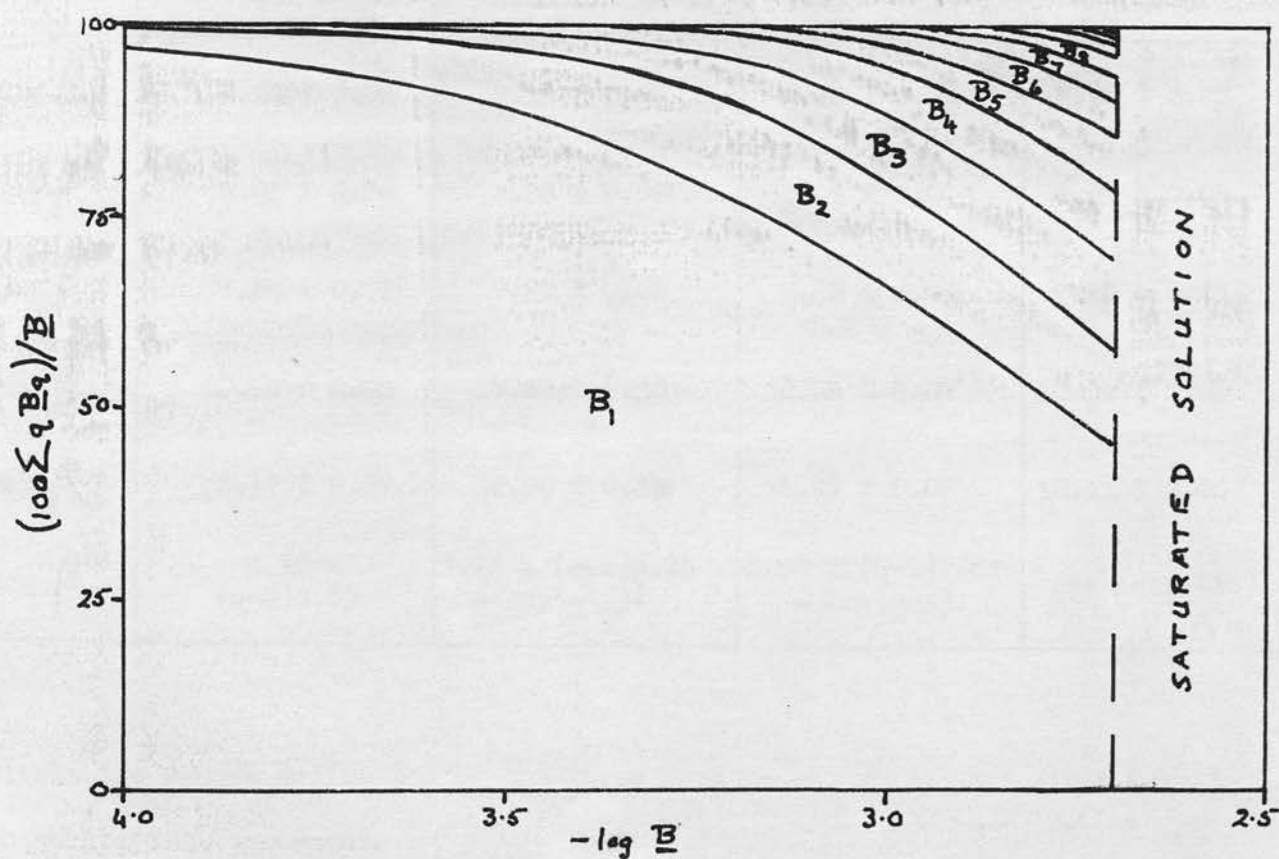


Fig. 9. The percentage distributions  $(100 \sum q_i B_i) / B$  of the 3,5-diphenylpyrazole species in carbon tetrachloride at  $21^\circ\text{C}$ ., plotted as a function of  $\log B$ .

oligomers of 3,5-dimethylpyrazole, calculated from the positions of best fit of the experimental curves and the normalised curves for Hypotheses I, III and IV, are given in Table 6. The errors are estimated from the permissible displacements of the experimental functions over the normalised curves parallel to the coordinate axes. Actual values of the equilibrium constants presumably lie

TABLE 6

Self-association Constants for the 3,5-diphenylpyrazole System

	Hypothesis I Eqns. (18), (20) and (21).	Hypothesis III Eqns. (20), (21) and (30).	Hypothesis IV Eqns. (20), (21) and (34).	Lassette Eqns. (38) and (39).
$\log \beta_{20}$	$2.19 \pm 0.05$	$2.18 \pm 0.04$	$2.15 \pm 0.04$	$2.23 \pm 0.03$
$\log \beta_{30}$	$5.01 \pm 0.04$	$5.08 \pm 0.06$	$5.06 \pm 0.04$	$4.91 \pm 0.03$
$\log \beta_{40}$	$7.83 \pm 0.05$	$7.80 \pm 0.08$	$7.85 \pm 0.06$	$7.70 \pm 0.04$
$\log \beta_{50}$	$10.65 \pm 0.06$	$10.40 \pm 0.10$	$10.58 \pm 0.07$	$10.54 \pm 0.04$
$\log \beta_{60}$	$13.47 \pm 0.07$	$12.90 \pm 0.12$	$13.29 \pm 0.08$	$13.41 \pm 0.05$
$\log \beta_{q0}$	$2.19 +$ $(q-2)2.82$	$2.18 + (q-2)3.20$ $- \log(q-1)!$	$2.15 + (q-2)2.61$ $+ \log(q-1)$	see eqn. (38)

within the ranges delineated by the three Hypotheses, which have given results in substantial agreement.

2) Lassette's method.<sup>14</sup> The only other two-parameter model in the literature was suggested by Lassette<sup>14</sup> in 1957. For a system  $\underline{B}(\underline{S})$ , which conforms to the linear equation

$(\underline{B} - \underline{S})/\underline{S}^2 = (\underline{C}_{\underline{B}}\underline{B}/\underline{S}) + \underline{C}_{\underline{S}}$ , (where the parameters  $\underline{C}_{\underline{B}}$  and  $\underline{C}_{\underline{S}}$  denote a functional dependence of  $\underline{B}/\underline{S}$  upon  $\underline{B}$  and  $\underline{S}$  respectively), it may be shown that

$$\beta_{q0} = \frac{\sum_{m=0}^{m=q-2} \left[ q \underline{C}_{\underline{B}} + (q-m) \underline{C}_{\underline{S}} \right]}{q!} \quad (58)$$

The  $\underline{B}(\underline{S})$  data for 3,5-dimethylpyrazole may be represented by the linear equation

$$(\underline{B} - \underline{S})/\underline{S}^2 = (610\underline{B}/\underline{S}) - 440 \quad (59)$$

Stability constants have been calculated by substituting the parameters of eqn. (59) into eqn. (38), and are reported in Table 6. It can be seen that they are in good agreement with the constants calculated from the curve fitting methods.

#### Discussion

The curve fitting methods for calculating the stability constants give convincing proof that the 3,5-diphenylpyrazole system in carbon tetrachloride exists as an equilibrium between monomer, cyclic dimer and higher linear oligomers. Due to the assumptions made to enable calculation of accurate values for  $\underline{S}$  and  $b$  from the experimental data of  $\underline{B}$ , e, the former would have been in error had any other equilibrium existed. No accurate fits between the experimental functions of  $\log T$  ( $\log b$ ) and  $\log \theta$  ( $\log b$ ) and the pairs of normalised curves would therefore have been obtained.

The percentage distribution of 3,5-diphenylpyrazole between the various oligomers has been calculated as a function of the total concentration,  $B$ , using the constants given in column 1 of Table 6, and eqn. (13). These data are shown in Fig. 9. Values of  $\beta_{q0}$  may be considered to be significant provided that the corresponding values of  $qB_q/B$  are significantly greater than zero. It is thus found that significant concentrations of all oligomers up to the decamer ( $q = 10$ ) are present in saturated solutions. This fact presumably explains the low solubility of 3,5-diphenylpyrazole ( $2 \times 10^{-5} M$ ) as compared to the previous three compounds studied (all  $> 1M$ ) in carbon tetrachloride at room temperature.

The stability constant for the cyclic dimer of 3,5-diphenylpyrazole (155) is greater than that of pyrazole (47.5) and 3,5-diethylpyrazole (110) but less than that of 3,5-dimethylpyrazole (284). A study of accurate molecular models shows that the benzene rings in the 3,5-diphenylpyrazole dimer interact to a greater extent than do the ethyl groups in the dimer of 3,5-diethylpyrazole. It is therefore concluded that the benzene rings probably exert a greater stabilising effect than the methyl or ethyl groups on the hydrogen bonds, but that this effect is counteracted to some extent by slight steric interaction between the benzene rings.

THE HYDROGEN BONDING OF IMIDAZOLE IN CARBON TETRACHLORIDE SOLUTION

The self-association of pyrazole in carbon tetrachloride solution results in the formation of cyclic, hydrogen-bonded dimers and trimers. Analogous cyclisations for imidazole are sterically impossible, due to the relative positions of the nitrogen atoms. Indeed, a consideration of bond angles suggests that any oligomer smaller than the decamer will have strained hydrogen bonds. A study was therefore undertaken to investigate the nature of imidazole oligomers in carbon tetrachloride solution.

A preliminary infrared spectroscopic examination of dilute solutions showed a fundamental N-H stretching mode at  $3485 \pm 5 \text{ cm.}^{-1}$  with a half-band width of  $20 \text{ cm.}^{-1}$ . The intensity of this band decreased with increasing total concentration,  $B$ , of imidazole. Concurrently, a broad, bonded N-H band of increasing intensity appeared in the region  $3400 - 2000 \text{ cm.}^{-1}$ . This broad band contained six major peaks at 3125, 3040, 2925, 2850, 2705 and  $2620 \text{ cm.}^{-1}$ . The weak C-H band at  $3120 \text{ cm.}^{-1}$  was completely masked. A quantitative study was accordingly made of the concentration dependence of intensity of the  $3485 \text{ cm.}^{-1}$  band.

Procedure

Imidazole solutions of concentration  $B > 4 \times 10^{-4} \text{ M}$  were prepared by semi-micro weighing. More dilute solutions were prepared by accurate dilution of a  $1.022 \times 10^{-5} \text{ M}$  stock solution. All solution temperatures were  $18^\circ \pm 1^\circ \text{C}$ .

It was impossible to confirm that the intensity of the fundamental N-H stretching band of the free monomer conformed to Beer's law, as the most

dilute solutions ( $\underline{B} \sim 10^{-4} \text{M}$ ) that could be studied were still slightly ( $\sim 5\%$ ) hydrogen bonded. The optics of the system were checked by confirming that the intensity of the  $3485 \text{ cm.}^{-1}$  band obeyed Lambert's law. Solutions with  $10^4 \underline{B} = 8.176, 8.743$  and  $10.22\text{M}$  were used in conjunction with the  $4.00$  and  $0.5000 \text{ cm.}$  cells. The results conformed to Lambert's law to within  $\pm 1\%$ .

The concentration dependence of the intensity of the  $3485 \text{ cm.}^{-1}$  band was then investigated. Details of the 15 solutions used ( $10^4 \leq \underline{B} \leq 4 \times 10^{-5} \text{M}$ ) are listed in Table 7.

#### Interpretation of the Data

Calculation of Concentration Variables.- The value of the apparent molar extinction coefficient,  $\epsilon_1$ , of the monomer at  $3485 \text{ cm.}^{-1}$  was obtained graphically as  $\lim_{\underline{B} \rightarrow 0} (\log I_0/I)/\underline{B}$ : only a short extrapolation was necessary to obtain the precise value  $\epsilon_1 = 224 \pm 2$ .

The free N-H band in associated solutions might be due to free monomer only or to the free end-groups of linear oligomers. In the pyrazole system, it was possible to distinguish between these possibilities using an argument based upon the law of mass action (see Table 2). This rigorous approach could not be applied to the imidazole system owing to the more extensive hydrogen bonding. However, a qualitative argument showed that the absorption was due to the end-groups of the oligomers. As compared with the pyrazole system, where the free N-H absorption was due to free monomer only, the intensity of the broad, bonded N-H band of imidazole increased as  $\underline{B}$  increased far more markedly than the intensity of the free N-H band decreased. (This may be appreciated by comparing Figs.

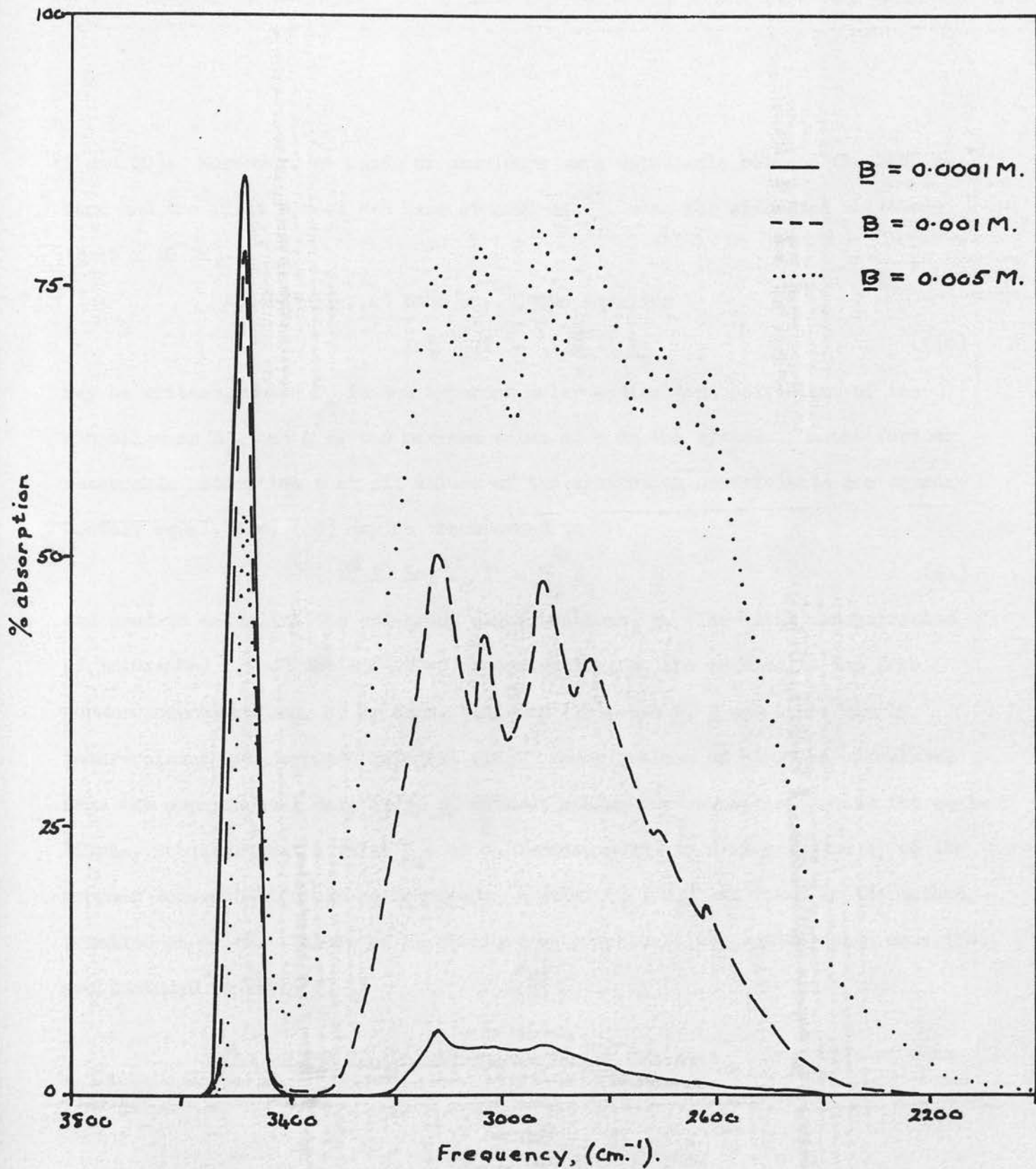


Fig. 10. Infrared absorption spectra in the region 3800-2000 cm.<sup>-1</sup> for carbon tetrachloride solutions of imidazole at various total concentrations,  $\underline{B}$ , at 18°C.

1 and 10). Moreover, no bands or shoulders were detectable between the 5485 cm.<sup>-1</sup> band and the first bonded N-H band at 3125 cm.<sup>-1</sup>, even for saturated solutions ( $\underline{B} \sim 5 \times 10^{-5} \text{M}$ ).

Accordingly, at 5485 cm.<sup>-1</sup>, the equation

$$\log I_0/I = 1 \sum_1^Q \epsilon_{q-1} B_q \quad (40)$$

may be written, where  $\epsilon_q$  is the apparent molar extinction coefficient of the qth oligomer  $B_q$ , and Q is the maximum value of q in the system. On the further reasonable assumption that all values of the extinction coefficients are approximately equal, eqn. (40) may be transformed to

$$(1/\epsilon_1) \log I_0/I = \sum_1^Q B_q = \underline{S} \quad (41)$$

and used to calculate the end-group concentrations,  $\underline{S}$ . The total concentration of imidazole,  $\underline{B}$ , and the end-group concentration,  $\underline{S}$ , are related to the free monomer concentration, b, by eqns. (13) and (15), and  $\underline{B}$ ,  $\underline{S}$  and b are simply inter-related by Bjerrum's integral (16). Hence, values of b may be calculated from the experimental data ( $1/\underline{B}$ ,  $\underline{S}$ ) without making any assumptions about the equilibria, provided that a value  $\underline{S}_1$ , of  $\underline{S}$ , corresponding to a known value  $b_1$  of the monomer concentration can be selected. A point ( $\underline{S}_1$ ,  $b_1$ ) was found by the method detailed on p. 92. Values of b, obtained by graphical integration using eqn. (16), are included in Table 7.

The Degree of Polymerisation of the System,- By combining eqns.

(15) and (15), we obtain

$$\underline{B}/\underline{S} = \sum_1^Q q B_q / \sum_1^Q B_q = \sum_1^Q M_{q-1} B_q / M_1 \sum_1^Q B_q = \bar{M}_n / M_1$$

where  $M_1$ ,  $M_q$  and  $\bar{M}_n$  are the monomeric molecular weight, the molecular weight of the qth oligomer, and the number average molecular weight respectively. The ratio

TABLE 7

Infrared Absorbancies at 3485 cm.<sup>-1</sup> of Associated Imidazole in Carbon Tetrachloride at 18° ± 1°C., and Concentration Variables derived therefrom

$10^4 \underline{B}$	$\log I_o/I$	$10^4 \underline{S}$	$\log b$	$10^4 \underline{B}$	$\log I_o/I$	$10^4 \underline{S}$	$\log b$
2.044	0.174	1.941	-3.718	10.22	0.670	7.473	-3.223
3.066	0.252	2.810	-3.584	12.78	0.098*	8.750	-3.174
4.088	0.325	3.628	-3.483	15.59	0.111*	9.937	-3.138
4.857	0.374	4.170	-3.430	20.62	0.130*	11.57	-3.102
6.132	0.462	5.158	-3.350	24.10	0.139*	12.37	-3.086
6.800	0.495	5.523	-3.325	31.19	0.157*	14.00	-3.060
8.176	0.578	6.455	-3.271	40.22	0.173*	15.41	-3.043
8.743	0.607	6.777	-3.255				

\* 5.000 mm. cells; all other results refer to 4.00 cm. cells.

$\underline{B}/\underline{S}$  is the number/average degree of polymerisation of the system, and may be obtained directly from the infrared measurements. In the restricted concentration range available to experiment, its value increased from unity to 2.60 (see Fig. 11). A better indication<sup>12,13</sup> of the nature of the oligomers present in solution is obtained by subtracting the monomeric term and calculating  $\bar{v}$ , the number average of monomers per oligomer. Values of  $\bar{v}$ , calculated using the equation

$$\bar{v} = (\underline{B} - b)/(\underline{S} - b) = \frac{\sum_2^Q qB_q}{\sum_2^Q B_q},$$

increased from ~2 to ~5, and increased sharply as saturation was approached,

IMIDAZOLE

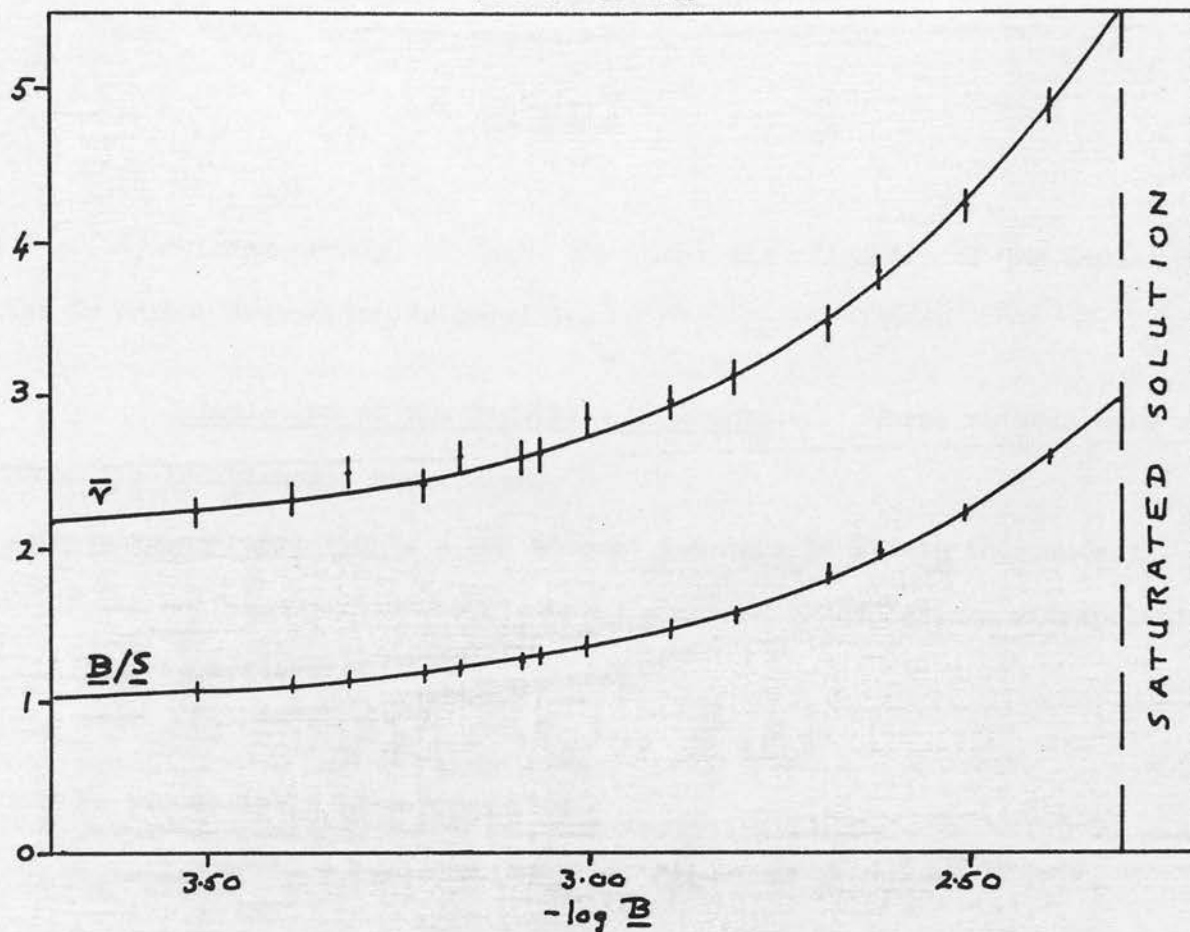


Fig. 11. The number average degree of polymerisation of the system,  $\underline{B/S}$ , and the average number of monomers per oligomer,  $\bar{v}$ , as functions of  $\log B$ .

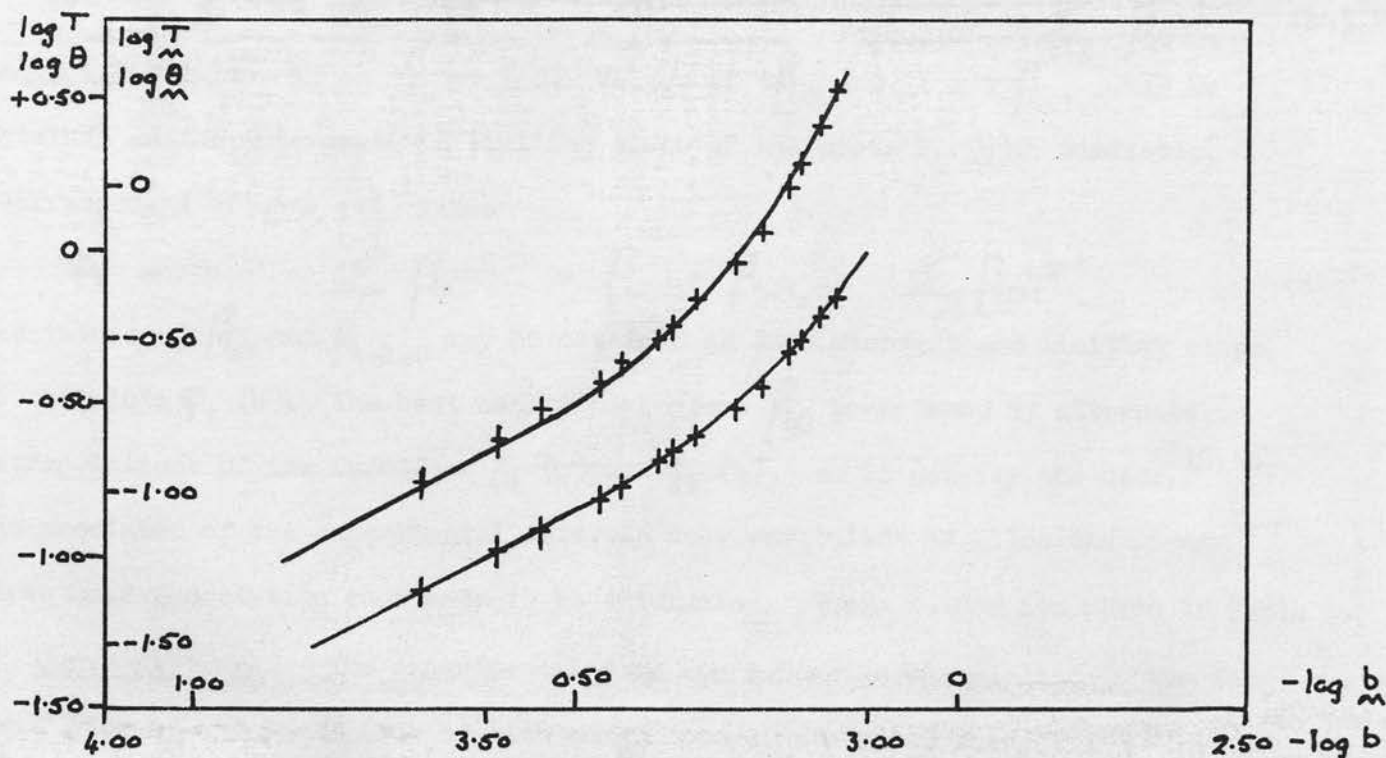


Fig. 12. The experimental data  $\log T(\log b)$  and  $\log \theta(\log b)$  superimposed in the position of best fit on normalised curves calculated using eqns. (22) and (25).

(see Fig. 11). Consequently, at least the first six oligomers of the series  $B_q$  coexist in carbon tetrachloride solution.

Calculation of the Stability Constants.- Three methods were used, and these are individually considered.

1) Successive extrapolations. An attempt was made to obtain independent values of the self-association constants by a method of successive extrapolations.<sup>12</sup>

Eqn. (13) may be written as

$$\underline{B} = b + 2\beta_{20}b^2 + 3\beta_{30}b^3 + \sum_4^Q q\beta_{q0}b^q .$$

This may be successively transformed to:

$$F_2 = (\underline{B} - b)/b^2 = 2\beta_{20} + 3\beta_{30}b + \sum_4^Q q\beta_{q0}b^{q-2} ,$$

$$F_5 = (\underline{B} - b - 2\beta_{20}b^2)/b^5 = 3\beta_{30} + \sum_4^Q q\beta_{q0}b^{q-5} , \text{ etc.},$$

or, in general,

$$F_t = \underline{B}b^{-t} - \sum_1^{t-1} q\beta_{q0}b^{q-t} = t\beta_{t0} + (t+1)\beta_{t+1,0}b + \sum_{t+2}^Q q\beta_{q0}b^{q-t} \quad (42)$$

where  $1 \leq q \leq (t-1)$  and  $2 \leq t \leq Q$ . Values of  $t\beta_{t0}$  and  $(t+1)\beta_{t+1,0}$  may be obtained as the intercept and limiting slope of the plots  $F_t(b)$ . Similarly,

rearrangement of eqn. (15) gives

$$\Phi_t = \underline{S}b^{-t} - \sum_1^{t-1} \beta_{q0}b^{q-t} = \beta_{t0} + \beta_{t+1,0}b + \sum_{t+2}^Q \beta_{q0}b^{q-t} \quad (43)$$

and values of  $\beta_{t0}$  and  $\beta_{t+1,0}$  may be obtained as the intercept and limiting slope of the plots  $\Phi_t(b)$ . The best set of parameters  $\beta_{q0}$  were found by alternate extrapolations of the functions  $F_t(b)$  and  $\Phi_t(b)$ . As is usually the case,<sup>12,13</sup>

the precision of the experimental data was only sufficient to allow the first three self-association constants to be determined. Their values are given in Table 8.

2) Curve fitting. The experimental data for imidazole was plotted in the form  $\log T(\log b)$  and  $\log \Theta(\log b)$  with common coordinate axes, where  $T$  and  $\Theta$  are

defined by eqns. (19) and (23). These functions were compared with the four pairs of normalised curves  $\log T_m(\log b)$  and  $\log \theta_m(\log b)$ , calculated for the models described on pps. 94 - 96. The experimental curves were found to be of the same shape as the pair of normalised curves calculated on the assumptions described in Hypothesis I (see Fig. 12). This hypothesis therefore provides a valid description of the imidazole system in carbon tetrachloride solution.

The values of the parameters  $\beta_{20}$  and K were found by solving eqns. (21), and (20) or (24) in the position of best fit (see Fig. 12). The limits of errors of these parameters were found from the permissible displacements of the experimental functions over the normalised curves parallel to the coordinate axes. In this way, it was found that

$$\log \beta_{20} = 2.57 \pm 0.03$$

and

$$\log K = 2.88 \pm 0.01 .$$

3) Lassettre's method. This is described on p. 98. It was found that the  $\underline{B}(\underline{S})$  data for imidazole could be represented by the linear equation

$$(\underline{B} - \underline{S})/\underline{S}^2 = (470\underline{B}/\underline{S}) - 170 . \quad (44)$$

Stability constants have been calculated by substitution of the parameters of eqn. (44) into eqn. (58).

### Discussion

Values of the first few self-association constants of the linear oligomers of imidazole, calculated by the various methods, are collected together in Table 8. Actual values of the equilibrium constants presumably lie within

TABLE 8

Self-association Constants for the Imidazole System obtained by Various Methods

	Eqn. (17).	Eqns. (42) and (43).	Eqns. (20) and (21).	Eqns. (38) and (44)
$\log \beta_{20}$	$2.45 \pm 0.03$	$2.38 \pm 0.02$	$2.37 \pm 0.03$	$2.48 \pm 0.04$
$\log \beta_{30}$		$5.23 \pm 0.03$	$5.25 \pm 0.04$	$5.20 \pm 0.04$
$\log \beta_{40}$		8.00	$8.13 \pm 0.05$	$8.02 \pm 0.05$
$\log \beta_{50}$			$11.00 \pm 0.06$	$10.89 \pm 0.05$
$\log \beta_{60}$			$13.89 \pm 0.07$	$13.78 \pm 0.05$
$\log \beta_{q0}$			$2.37 + (q-2)2.88$	see eqn. (38)

the ranges delineated by the various methods, which have given results in substantial agreement.

The percentage distribution of imidazole between the various oligomers has been calculated as a function of the total concentration,  $\underline{B}$ , by using the constants obtained by curve fitting and eqn. (13). These data are shown in Fig. 13. Subject to the assumptions of the model, values of  $\beta_{q0}$  may be considered significant provided that the corresponding values of  $q\underline{B}_q/\underline{B}$  are significantly greater than zero. It is thus found that significant concentrations of all oligomers up to the dodecamer ( $q = 12$ ) are present in saturated solutions.

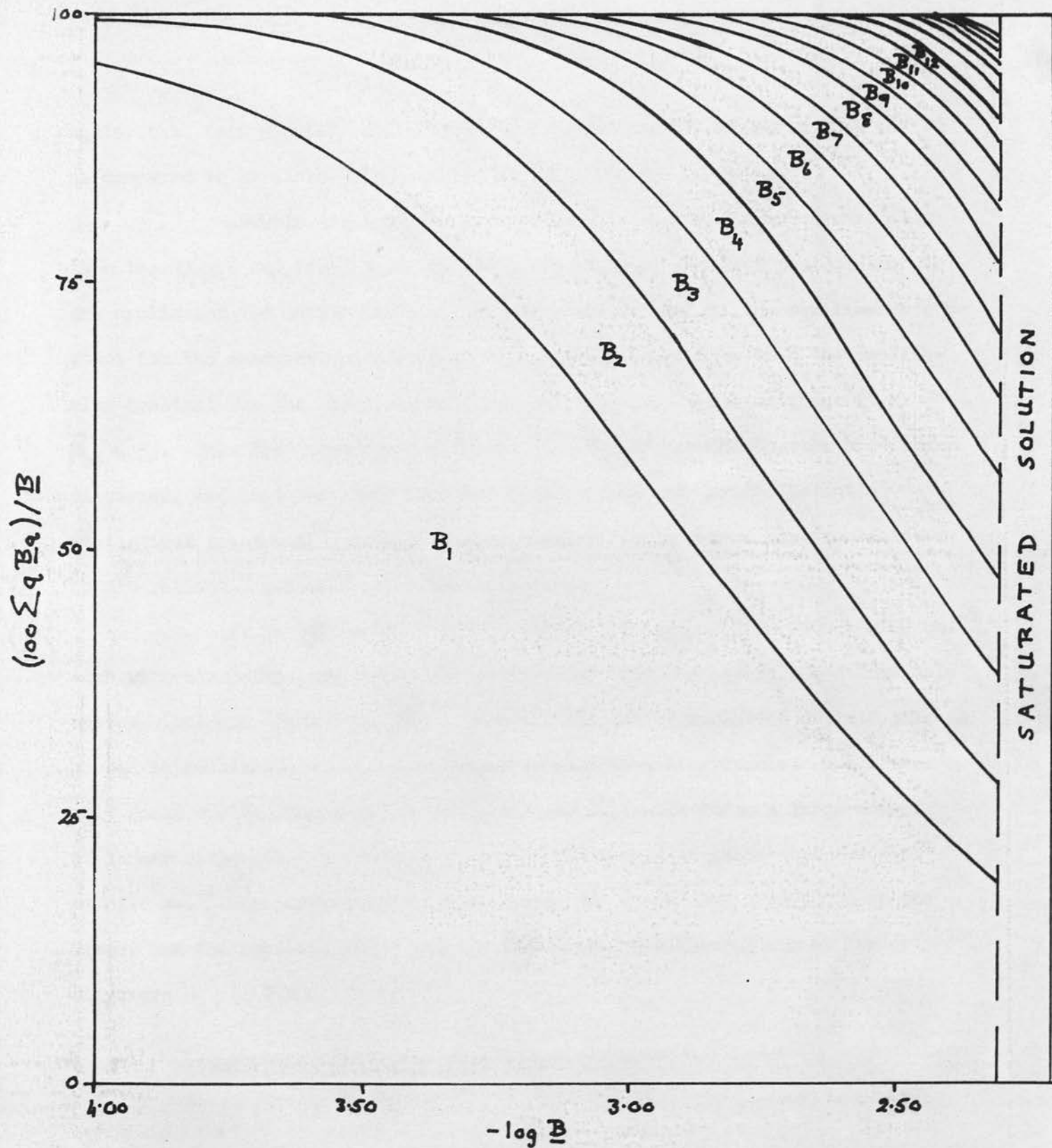


Fig. 13. The percentage distributions  $(100 \sum q B_q) / B$  of the imidazole species in carbon tetrachloride at  $18^\circ\text{C}$ ., plotted as a function of  $\log B$ .

Again, this fact possibly explains the low solubility of imidazole ( $5 \times 10^{-3}M$ ) as compared to pyrazole ( $>1M$ ) in carbon tetrachloride at  $18^{\circ}C$ .

Dimeric and trimeric pyrazole are less stable thermodynamically than the dimers and trimers of imidazole, in spite of the fact that the former are cyclic and the latter linear. In the imidazole system, the equilibrium constant for the association of monomer with monomer is smaller than the equilibrium constant for the association of monomer with any larger oligomer (i.e.  $\beta_{20} < K$ ). This fact also applies to the 3,5-diphenylpyrazole system previously discussed, and is to be expected, both on the grounds of Saroléa-Mathot's statistical treatment<sup>15</sup> concerning the entropy term and from electrostatic considerations<sup>16</sup> concerning the enthalpy term.

It is noteworthy that the bonded N-H regions from  $3400 - 2000 \text{ cm.}^{-1}$ , each with six peaks, are remarkably similar for both the pyrazole and imidazole systems (compare Figs. 1 and 10). However, the self-association of imidazole in carbon tetrachloride is far more extensive than that of pyrazole. The latter only forms cyclic dimers and trimers, whereas imidazole forms a large number of linear oligomers. A comparison of Figs. 10 and 13 suggests that the peak at  $3125 \text{ cm.}^{-1}$  may tentatively be assigned to the bonded N-H absorption of the dimer, and the remaining five peaks to the bonded N-H absorptions of larger oligomers  $B_q$ , ( $q > 2$ ).

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**THE IDENTIFICATION AND QUANTITATIVE ESTIMATION OF GAS-CHROMATOGRAPHY FRACTIONS BY VAPOUR-PHASE INFRARED SPECTROSCOPY**

By *D. M. W. Anderson and J. L. Duncan*

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For reasons now well-known,<sup>1,2</sup> identification of gas-chromatography fractions based solely on relative column retention-times can be dangerously inadequate and ambiguous. Confirmation of fraction homogeneity and unequivocal identification of eluted solutes by a fundamental method such as mass spectrometry<sup>3</sup> or infrared spectroscopy<sup>4</sup> is always desirable but not often possible, since only microgram quantities of each fraction may be recovered from the column.

Recently, spectroscopists have been developing scale-expansion and beam-reduction techniques to facilitate identification of microgram quantities: for certain types of spectrometer, liquid cells of 0.1 microlitre volume are now commercially available.

For volatile liquids of low or medium boiling-point, however, it appeared that their examination as vapours would be much more convenient experimentally. More accurate quantitative estimations would result from the elimination of volatility losses during transfer from trap to cell, etc., and the samples could be quantitatively recovered after examination.

Gas-cell "A" (see Table I) has been used in this laboratory during the past two years in a simple but

Table I

	Cell "A"	Cell "B"	Cell "C"
Approx. diameter (cm.)	2.3	1.5	1.5
Approx. length (cm.)	12.5	31.5	56.0
Actual internal vol. (ml.)	58.0	51.5	110.0
Useful concn. range (moles)	min. $4 \times 10^{-6}$	10 <sup>-7</sup>	10 <sup>-9</sup>
	max. $5 \times 10^{-5}$	$4 \times 10^{-6}$	10 <sup>-7</sup>
Accuracy of estimation	$\pm 1\%$	$\pm 1.5\%$	$\pm 2\%$
B.p. limitation (approx.)	$\nabla 175^{\circ}\text{C.}$	$\nabla 125^{\circ}\text{C.}$	$\nabla 125^{\circ}\text{C.}$

effective technique which has been described.<sup>1</sup> A useful design feature of the Hilger H800 spectrometer is the length of gas-cells which can be positioned in the sample and reference beams. It has now been found possible, using unheated conventional gas-cells "B" and "C" of circular cross-section and the dimensions shown in Table I, to extend the sensitivity of the method to the identification and quantitative estimation of as little as 10<sup>-9</sup> moles, thus matching the sensitivity of many G.L.C. columns.

It is proposed to publish full experimental details (and results from an investigation, at present in progress, into the use of heated cells to extend applicability to liquids of higher boiling point) in due course.

We thank Prof. E. L. Hirst, F.R.S., for his interest in this work and the Carnegie Trust for the award (to J. L. D.) of a Research Scholarship.

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## ANOMALOUS REACTIONS IN THE ZEISEL ALKOXYL DETERMINATION

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Although Steyermark<sup>1</sup> has recommended caution in interpreting Zeisel alkoxy results, few specific examples of compounds which produce methyl iodide anomalously appear to have been reported, other than (a) non-alkoxy polyhydric alcohols<sup>2</sup> and (b) *N*-methyl compounds such as 1:2-dimethylpyridazine-3:6-dione, which Gysel<sup>3</sup> suggested rearrange to methoxy compounds under alkoxy determination conditions.

Recently, we have investigated certain aspects of the micro-Zeisel reaction with the aid of infrared spectroscopy. By using suitable gas-cells<sup>4,5</sup> under standard conditions, approximately 1 mg. quantities of the lower alkyl iodides can be determined within  $\pm 1\%$ . Under the standard reaction conditions used (2-5 mg. substance dissolved in molten phenol, heated under reflux with 6 ml. constant-boiling HI (M.A.R.) for 1 hour, using nitrogen as carrier-gas at 6-8 ml./min. flow-rate) the *N*-methyl groups in ephedrine, atropine, narcotine and codeine phosphate are not attacked. The Table shows results obtained for the methoxyl content of the latter two compounds and for vanillin. Fifteen other compounds, analysed as "unknowns" (by J.L.D.) were determined with similar accuracy, which equals that of the iodometric method. This quantitative infrared technique has the tremendous added advantage of revealing simultaneously which of the alkoxy groups, or combination thereof, is present in an unknown compound: any of the lower alkyl iodides can be determined in presence of any of the others. Furthermore, while ethers yield only alkyl iodide, esters produce in addition measurable quantities of carbon dioxide<sup>6</sup>; it is hoped that this, in conjunction with kinetic data, will make differentiation between esters and ethers in the Zeisel reaction possible.

During kinetic studies on this effect, Ehrlich-Sachs esters<sup>7</sup> (prepared by condensation of *p*-nitroso-*N*-di-alkylanilines with cyanoacetic esters and kindly provided by Prof. F. Bell) were found to give the

anomalous alkoxy values shown in the Table. *p*-Nitroso-dimethylaniline (twice recrystallised from diethyl ether) itself gives an apparent methoxyl content; in such compounds the *N*-methyl group is apparently sufficiently liable to react partially under alkoxy determination conditions.

During similar experiments with several phenolic anti-oxidants, (kindly provided as a gift by Eastman-Kodak, Kirkby, Liverpool) *tert*-butylated-*p*-hydroxy anisole (mixed 2- and 3-isomers) gave approximately 0.5 moles *tert*-butyl iodide in addition to 1 mole of methyl iodide; 2:6-di-*tert*-butyl-*p*-cresol also gave 0.5 moles *tert*-butyl iodide. Since *tert*-butyl groups are easily removed from a substituted benzene nucleus, particularly when other strongly *ortho/para* directing substituents are present,<sup>8,9</sup> the formation of *tert*-butyl iodide is not surprising. Whilst modifications involving (a) the reaction period involved<sup>10</sup> and (b) use of hot water on traps<sup>11</sup> and in the reflux condenser<sup>12</sup> have been found necessary to give quantitative yields of iodides from propoxy and butoxy compounds, *tert*-butyl iodide is sufficiently volatile, even with a rapid flow of very cold condenser water, to produce anomalous results in the determination of *tert*-butylated alkoxy compounds.

We thank Prof. E. L. Hirst, F.R.S., for his interest, and the Carnegie Trust for the award (to J.L.D.) of a Research Scholarship.

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Compound	Theoretical		Found*	
	% OMe	% OEt	% OMe	% OEt
Narcotine	22.5	—	22.7, 22.2	—
Codeine Phosphate	7.31	—	7.16, 7.19	—
Vanillin	20.4	—	20.3, 20.4, 20.3, 20.5	—
Phenacetin	—	25.1	—	25.0, 24.9
<i>p</i> -nitroso- <i>N</i> : <i>N'</i> -dimethylaniline	0	—	2.0, 4.0 (2.5 hours) 4.5 (3 hours)	—
<i>p</i> -nitroso- <i>N</i> -methylaniline	0	—	3.3, 6.3 (2 hours)	—
Compounds of type R' <sub>2</sub> N.σ.N=C(CN)CO <sub>2</sub> R'':				
(a) R'=R''=Me, σ=C <sub>6</sub> H <sub>4</sub>	13.4	—	14.1, 14.7 (2 hours)	—
(b) R'=R''=Me, σ=C <sub>6</sub> H <sub>3</sub> .Me	12.7	—	13.4, 14.1 (2 hours)	—
(c) R'=Me, R''=Et, σ=C <sub>6</sub> H <sub>4</sub>	0	18.4	2.7	18.2
(d) R'=Et, R''=Me, σ=C <sub>6</sub> H <sub>3</sub> .Me	11.4	0	11.4	2.5
(e) As for (a), but C <sub>6</sub> H <sub>5</sub> for CO <sub>2</sub> R''	0	—	2.0	—

\*Reflux period=1 hour, except where stated.

## SOLID SCRUBBERS IN THE ZEISEL ALKOXYL DETERMINATION

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Since the Zeisel method was first described,<sup>1</sup> at least sixteen different scrubbing solutions, suspensions and combinations thereof have been proposed. Although the disadvantages of some of these are now well known,<sup>2, 3</sup> difficulty in obtaining quantitative results, particularly when sulphur is present,<sup>4</sup> is still encountered in some cases.

Quantitative vapour-phase infrared spectroscopy permits the determination of lower alkyl iodides not only in presence of each other,<sup>5</sup> but also in presence of other volatile reaction products, e.g. H<sub>2</sub>S. Before collection in a cold trap,<sup>6</sup> the volatile products are passed only through anhydrone, in which only water vapour is retained. The results listed below are representative of a wide range of alkoxy/sulphur compounds, and of alkoxy compounds assayed in presence of added inorganic sulphate; other results presented recently<sup>5</sup> were obtained in the same way. Thus within the limits of accuracy claimed ( $\pm 1\%$ ) no detectable interaction between alkyl iodides and other reaction products occurs in the vapour phase.

Interaction in aqueous scrubbing solutions, resulting in loss of alkyl iodides, can however occur.<sup>7</sup> Whilst such effects were under investigation, (during which results substantiating those of earlier authors<sup>2, 3, 7, 8</sup> were obtained), we investigated the possibility of using a solid scrubber in alkoxy determinations. Such a scrubber, it appears, was first used by Fierz-David.<sup>9</sup> We have obtained good results for all C<sub>1</sub>-C<sub>4</sub> alkoxy groups (each in presence of added inorganic sulphate) using as scrubber soda asbestos (B.D.H., M.A.R.) which quantitatively

absorbs H<sub>2</sub>S, HI, I<sub>2</sub> and CO<sub>2</sub> but does not retain alkyl iodides. In contrast, "Natronasbest" was reported<sup>10</sup> to give unsatisfactorily high blank values and results, for which, however, no explanation was given. Ascarite was successfully used by Filipovic and Stefanac,<sup>11</sup> with whom we agree in general regarding the considerable advantages gained by the use of a suitable solid scrubber.

Studies of other aspects of the Zeisel determination continue.

### Acknowledgment

We thank Prof. E. L. Hirst, C.B.E., F.R.S., for his interest, and the Carnegie Trust for the award (to J.L.D.) of a Research Scholarship. Gifts of compounds from Dr. G. O. Aspinall (Nos. 7 & 8), Prof. F. Bell (No. 6), Baywood Chemicals Ltd. (No. 3) and I.C.I. Ltd. (No. 4) are gratefully acknowledged.

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### Results

Compound	Molecular Formula	mg. taken	mg. Na <sub>2</sub> SO <sub>4</sub> added	% Alkoxy	
				Theory	Found
1. Dimethyl sulphate	C <sub>2</sub> H <sub>6</sub> SO <sub>4</sub>	3.86	—	49.2 OMe	49.0
2. Papaverine sulphate	C <sub>20</sub> H <sub>21</sub> NO <sub>4</sub> .H <sub>2</sub> SO <sub>4</sub>	1.54	—	28.4 OMe	28.6
		1.82	—		28.2
3. "Gusathion"*	C <sub>10</sub> H <sub>12</sub> N <sub>3</sub> O <sub>3</sub> PS <sub>2</sub>	7.72	—	19.6 OMe	19.4
4. 4-aminoanisole-3-sulphonic acid	C <sub>7</sub> H <sub>9</sub> NO <sub>4</sub> S	7.76	—	15.3 OMe	15.3
5. O:O':O''-triethyl-phosphorothioate	C <sub>6</sub> H <sub>15</sub> O <sub>3</sub> PS	1.31	—	68.2 OEt	67.8
6. 6-bromo-2-ethoxy-N-toluene-p-sulphonyl-1-naphthylamine.	C <sub>19</sub> H <sub>18</sub> NO <sub>3</sub> SBr	6.72	—	10.7 OEt	10.6
7. Methyl-4:6-O-benzylidene- $\alpha$ -D-glucoside-2-toluene-p-sulphonate	C <sub>21</sub> H <sub>24</sub> O <sub>8</sub> S	7.90	—	7.12 OMe	7.06
8. Methyl-4:6-O-ethylidene- $\alpha$ -D-mannoside-3-nitrate-2-toluene-p-sulphonate	C <sub>16</sub> H <sub>21</sub> O <sub>10</sub> NS	8.56	—	7.41 OMe	7.41
9. Vanillin (M.A.R.)	C <sub>8</sub> H <sub>8</sub> O <sub>3</sub>	2.90	15	20.4 OMe	20.5
		3.00	30		20.4
10. Phenacetin (M.A.R.)	C <sub>10</sub> H <sub>13</sub> O <sub>2</sub> N	3.01	15	25.1 OEt	25.2
		3.06	30		25.2
11. n-propyl-3:5-dinitrobenzoate	C <sub>10</sub> H <sub>10</sub> O <sub>6</sub> N <sub>2</sub>	6.00	30	23.2 OPr	23.1
		5.79	60		23.3
12. n-butyl-3:5-dinitrobenzoate	C <sub>11</sub> H <sub>12</sub> O <sub>6</sub> N <sub>2</sub>	3.15	15	27.3 OBU	27.5
		3.03	30		27.3

\* "Gusathion": S-(1:2:3:4-tetrahydro-6-oxo-benzo-1:2:3-triazin-2-yl)-methyl-O:O-dimethyl-phosphorothiolothionate.

## APPLICATIONS OF INFRARED SPECTROSCOPY—II\*

### OBSERVATIONS ON SOME ASPECTS OF THE ZEISEL ALKOXYL DETERMINATION

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(Received 30 June 1960)

**Summary**—A sensitive infrared method for quantitative determination of vapours has been used to study some of the reaction variables in the Zeisel alkoxy determination. Several conflicting reports in the literature have been clarified. Reaction conditions giving rapid and accurate determinations on solids and volatile liquids, even in presence of large sulphur concentrations, are described: for determinations on vanillin the standard deviation is 0.16%. Interaction between alkyl iodides and sulphuretted hydrogen has been found to occur only in aqueous solutions; the use of soda-asbestos as a solid scrubber therefore has fundamental advantages over aqueous solutions, and gives excellent results.

ALTHOUGH the determination of alkoxy groups is still based on Zeisel's classical method,<sup>1</sup> an iodometric procedure<sup>2</sup> has largely superseded the original gravimetric technique. In addition, an almost continuous catalogue of modifications to procedure, reagents, scrubber composition and apparatus design has been published. (See, for instance, references 3, 4, 5, 6, 7, 8, 9 and 10.) Since conflicting recommendations and statements still exist in the literature, an attempt to clarify the present position seemed desirable.

#### METHOD OF INVESTIGATION

A sensitive infrared technique,<sup>11,12</sup> developed recently for the quantitative determination of substances in the vapour phase, has been used to study certain stages of the alkoxy determination. Milligram-quantities of the lower alkyl iodides can be trapped quantitatively in liquid nitrogen<sup>11</sup> and can subsequently be determined by referring the heights of selected characteristic peaks in their infrared spectrum to a carefully constructed calibration curve. This is previously obtained under carefully standardised spectroscopic conditions by quantitatively volatilising weighed amounts of purified alkyl iodides into the infrared gas-cell. (Experimental details of the procedures involved will be given in a subsequent paper<sup>35</sup> describing an infrared method for the simultaneous determination of methoxy and ethoxy groups.) Other vapours, *e.g.* hydrogen sulphide, hydrogen iodide and iodine, do not interfere with the determination since there is (*a*) no reaction between these and alkyl iodides in the vapour phase, and (*b*) no overlapping of peaks in their infrared spectra.

Since it is necessary in infrared spectroscopy to exclude water-vapour, the volatile reaction products are trapped after passage through Anhydrone; an Anhydrone guard-tube must be fitted to the trap, as shown in Fig. 1. Careful preliminary tests showed that, of the normal volatile reaction products, Anhydrone retained only water-vapour.

\* Part I: D. M. W. Anderson, *Analyst*, 1959, **84**, 50.

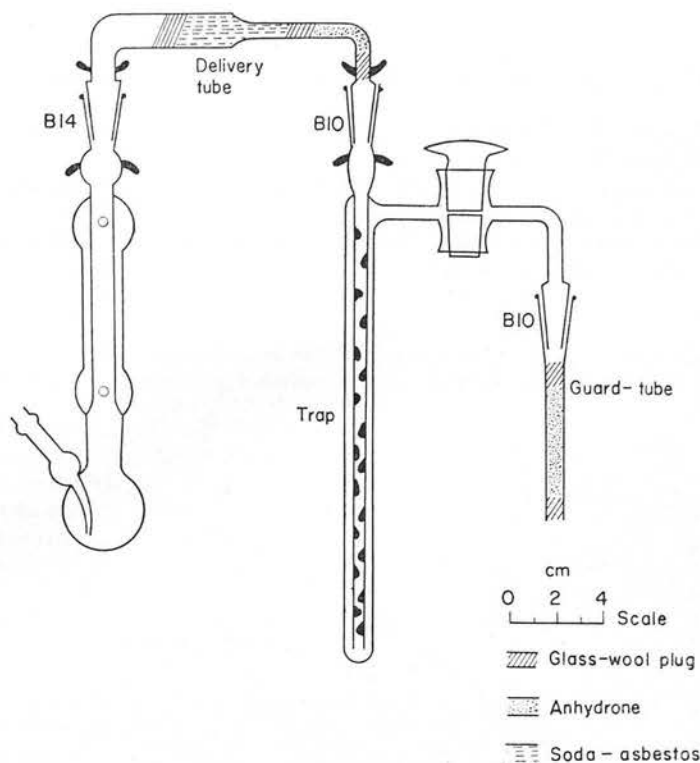


FIG. 1. Assembled apparatus.

The reaction products could therefore be trapped either before or after passage through scrubbers or absorbers of the type normally used in Zeisel determinations. The subsequent spectroscopic examination not only revealed which alkyl iodide had been produced and permitted simultaneous measurement of its concentration, but also revealed if any other volatile product affecting the validity of the result had been produced. The high sensitivity and adequate accuracy of this infrared technique conveniently gave information on (a) efficiency of removal of hydrogen sulphide by scrubbers (b) sources of loss of alkyl iodide, and (c) anomalous reaction of certain compounds.

#### EXPERIMENTAL

##### Reagents

*Hydriodic acid*: M.A.R., sp. gr. 1.7 (6-ml ampoules).

*Phenol*: AnalaR.

*Anhydron*: M.A.R., 14–22 mesh.

*Soda-asbestos*: M.A.R.

*Alkyl iodides*: for calibration purposes, the reagent grade was re-distilled three times; the still-head was packed with Anhydron and the middle fraction collected each time.

##### Standard compounds

*α-Methyl-D-glucoside*

*Vanillin*  
*Phenacetin* } organic analytical standards.

In addition, *vanillin* (microanalytical standard grade) purified by zone-melting was used.

### Apparatus

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

(a) the combined reaction-flask and condenser described in B.S. 1428: part C 1:9154 (type-2 apparatus).

(b) a delivery-tube, which could be packed with Anhydrone and soda-asbestos. Ground-glass joints were lightly coated with silicone grease.

(c) a trap, similar to that previously described.<sup>11</sup> Recent traps have been made with Vigreux-type indentations in the inner absorption tube, as shown in Fig. 1.

(d) the design of scrubber described in B.S. 1428: part C 1:1954 was used to investigate the efficiency of aqueous scrubbing solutions.

### Calibration curves

Fig. 2 shows a typical calibration curve, constructed by making about 5 different measurements per 5-mg range of alkyl iodide using a Hilger double-beam infrared spectrometer. The gas-cells described

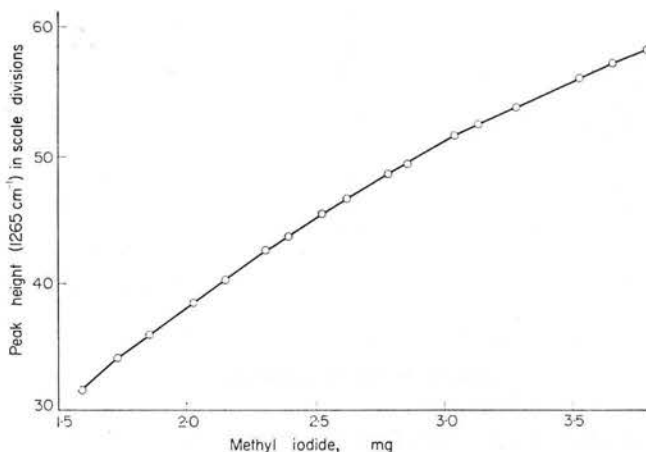


FIG. 2. Calibration curve for determination of methyl iodide.

in references 11 and 12 were used: gas-cells "A" (length 12.5 cm) and "B" (length 31.5 cm) respectively permitted determination of 4–10 mg and 1–4 mg quantities of methyl iodide.

### Weighing of samples

For solids, a long-handled weighing-spoon<sup>10</sup> was used. Volatile liquids were conveniently weighed in a long-handled micro weighing-bottle<sup>10</sup> fitted with a leak-proof ground-glass stopper.

### Flow-gas

The infrared technique required nitrogen to be used. Nitrogen ("N.O.F." grade) was passed through soda-asbestos, silica gel and Anhydrone. The flow-rate, stabilised by needle-valves and passage through a large reservoir fitted with capillary outlet, was adjusted by a Rotameter, Type 704, calibrated over the range 4–25 ml per min.

### Heating of reaction-flask

An electrothermal flexible heating mantle, Type MBJ 1822, gave very steady ebullition. Recent papers<sup>13</sup> still report difficulty with "bumping", although electrical heating was earlier reported to be advantageous.<sup>14</sup>

### Preliminary determinations using standards

(a) *Conditioning of acid and apparatus:* The contents of one 6-ml ampoule of hydriodic acid was added to the reaction flask and refluxed for 30 min under a steady flow of nitrogen (6–8 ml per min).

This procedure is advisable: it conditions the apparatus, ensures that the acid is constant-boiling, and decomposes any excess hypophosphorous acid which may have been added. (In any infrared investigations, all traces of phosphine must be removed, since its absorption peaks overlap the particular alkyl iodide peaks used for determination).

(b) *Determination of reaction-times and optimum flow-rate:* Recommended flow-rates have varied between 4<sup>7,15</sup> and 25<sup>8</sup> ml per min. For 2–5 mg samples and a flow-rate of 6–8 ml per min, we obtained quantitative recovery of methyl iodide from vanillin in 10–15 min and of ethyl iodide from phenacetin in 15–20 min from start of reflux. These times vary little from those found by Kirsten<sup>8</sup> (25 ml per min) and by Inglis<sup>9</sup> (12–15 ml per min). Since some compounds could possibly react more slowly than these standards, a reflux period of 30 min was adopted for methoxyl and ethoxyl compounds, and has since proved adequate for many organic compounds containing a wide range of other functional groups and analysed as "unknowns" by one of us (J. L. D.)

Although Inglis used carbon dioxide flow-gas at 12–15 ml per min with one scrubber (to minimise the tendency for methyl iodide to dissolve in aqueous solution), it had earlier been established<sup>10</sup> that a flow-rate of 6 ml per min caused high results if a second scrubber was not used. Pending investigation of these conflicting reports of scrubber efficiency, we considered that, since the reaction-times quoted above were sufficiently short for routine analyses, and were not in any case decreased appreciably by using faster flow-rates, the use of a slow flow-rate was fundamentally correct experimentally in minimising tendencies towards (a) inadequate gas scrubbing, and (b) incomplete alkyl iodide retention in the final stage. Any scrubber solution in which alkyl iodides react or are appreciably soluble at low flow-rates is unsatisfactory in any event. A flow-rate of 6–8 ml per min was therefore adopted as standard.

(c) *Results:* Table I shows the results obtained for standard compounds. This gives a true representation of the poorest results that may be expected, since none of the results obtained was rejected; the standard deviation is also shown.

TABLE I. RESULTS OF ALKOXYL DETERMINATIONS ON STANDARD COMPOUNDS

Compound	Range of sample weights taken, mg	No. of detns.	Alkoxy content		Stand. Devn., %	Max. divergence from theory	
			Theory, %	Av. found, %		+	-
Vanillin	1.84–3.39	15	20.40	20.39	0.16	0.28	0.28
$\alpha$ -Methyl-D-glucoside	2.38–4.36	5	15.99	15.99	0.08*	0.11	0.07
Phenacetin	2.82–3.67	6	25.15	25.18	0.17*	0.20	0.23

\* Calculated by the range method.

Having established that the reaction conditions described and the spectroscopic method of determining alkyl iodides gave satisfactory analyses of pure reference compounds, the following investigations were made.

## INVESTIGATIONS

### 1. Concentration and colour of hydriodic acid

Most analysts have found constant-boiling hydriodic acid adequate, but the use of more concentrated acid (sp. gr. 1.96) has been proposed,<sup>16</sup> and the addition of a few drops of this concentration to the constant-boiling acid suggested.<sup>5</sup> Reflux for 30 min over red phosphorus before use has been recommended.<sup>6,17</sup> We have found the M.A.R. constant-boiling acid, conditioned as already described, to be satisfactory; tests showed that, at 6–8 ml per min, only trace amounts, if any, of hydriodic acid vapour were volatilised. The use of more concentrated acid would give increased amounts of distilling acid vapour, so introducing a possible source of error.

Furter<sup>4</sup> stated that the use of fresh colourless acid was essential. Steyermark,<sup>18</sup> however, found that the colour was not critical if the acid was refluxed before use: more recently it was observed<sup>19</sup> that the presence of free iodine in the hydriodic acid was in fact advantageous. Belcher<sup>7</sup> obtained acceptable results titrimetrically in the presence of 20 mg added iodine, although an increased blank was observed. Our experiments confirm that the acid colour has no effect on the yield of alkyl iodide. Appreciable volatilisation of iodine does, however, occur from very dark mixtures, particularly if the compound under analysis contains sulphur or strong reducing groups, or, as can occur with carbohydrate materials, is readily decomposed to give carbon. As Kirsten pointed out,<sup>8</sup> this may impose an additional test on the scrubber efficiency, although much of the iodine condenses out before reaching the scrubber.

### 2. Repeated use of acid in routine analyses

In routine analyses when compounds are known to decompose quantitatively in the normal reaction-time, one charge of acid can safely be used for 8 determinations (av. sample weight = 5 mg) if the mixture is refluxed between each determination: to allow a safety margin, we have always used a reflux period of 30 min, but a shorter period may be found adequate. In one series of experiments, 14 successive determinations were satisfactorily made without change of acid. Care must always be exercised, however: we have found certain compounds<sup>20</sup> which liberate alkyl iodides continuously for several hours.

### 3. Determinations on volatile liquids

Earlier investigations found double distillation<sup>9,18,21</sup> or the use of modified apparatus<sup>8</sup> necessary for quantitative results. Double distillation is not essential when the following procedure is used:—

Weigh the sample as already described. Transfer to a reaction flask charged with a mixture of hydriodic acid (6 ml) + phenol (approximately 0.25 g) which has been conditioned as described for 30 min, then allowed to cool completely. The small stoppered weighing-bottle must submerge completely in the phenol-hydriodic acid mixture. Shake the reaction flask to loosen the weighing-bottle stopper. Using a nitrogen flow-rate of 2–4 ml per min, heat gently so that reflux begins after 8 to 10 min, then increase the flow-rate to 6 to 8 ml per minute and reflux for 30 minutes.

Compounds such as methanol, anisole, 1:1- and 1:2-dimethoxyethanes, and ethyl orthoformate have been analysed without difficulty in this way. Infrared experiments with anisole revealed that no detectable traces of unreacted anisole were volatilised together with the methyl iodide unless the flow-rate was increased to >15 ml per min.

### 4. Effect of presence of sulphur

The presence of sulphur has long been known to complicate alkoxy analyses, causing low results. Sulphur present in organic functional groups is usually reduced to hydrogen sulphide by reflux with hydriodic acid; inorganic sulphate reacts similarly. Commonly only 1 sulphur atom is present, but the ratio of sulphur atoms to alkoxy groups in compounds can exceed 1:1. It is of importance that the analysis of compounds mixed with relatively large amounts of inorganic sulphate has caused particular difficulty.<sup>22,23</sup>

An interaction between hydrogen sulphide and alkyl iodides, resulting in mercaptan formation,<sup>1,24</sup> is considered to cause the low results; Bethge and Carlson<sup>25</sup> suggested

that this reaction is favoured in alkaline solution. The infrared technique has shown that *no* reaction between hydrogen sulphide and alkyl iodides occurs in the vapour phase: alkoxy compounds containing sulphur, or to which had been added sodium sulphate, gave theoretical yields of alkyl iodide in presence of the evolved hydrogen sulphide. The undesired interaction must therefore occur only *in aqueous solution*.

Mere absorption of hydrogen sulphide by scrubbing solutions is therefore insufficient; quantitative removal of sulphide ions from solution in a rapid reaction is essential. Scrubbers must also effectively remove iodine and hydrogen iodide vapours: although the use of (a) low flow-rates, and (b) pre-conditioning of the hydriodic acid should ensure that the amounts of these involved are normally very small, there will be a tendency for increased volatilisation of iodine when much hydrogen sulphide is released. Thus any scrubber able to remove satisfactorily the large amounts of hydrogen sulphide liberated when excess inorganic sulphate is present will have a safety-factor when sulphur-containing organic compounds are analysed. The following investigation of scrubber efficiency was made from this viewpoint.

### 5. The efficiency of aqueous scrubbing solutions

The functional efficiency of the design of scrubber used must also be considered here; the volume of scrubbing solution and the flow-rate used will be contributing factors. The efficiencies of some scrubbing solutions were therefore initially compared at a flow-rate of 6–8 ml per min, 4 ml of the solution being used in the B.S. (1954) design spiral scrubber.

Our results confirmed<sup>10</sup> that aqueous sodium thiosulphate is unsatisfactory because of reaction with methyl iodide.<sup>26,27</sup> Table II summarises the other results obtained. For each solution tested, several determinations were made under the conditions shown; the range of recoveries obtained is quoted, since averaged results at the 100% level can be misleading.

(a) *In absence of sulphur*, all the solutions listed were satisfactory. Water itself, however, gave slightly low results; this is in agreement with Heron *et al.*,<sup>10</sup> who reported 94–98% recovery. These negative errors are undoubtedly due to the solubility of methyl iodide in water; the effect can be minimised by keeping the scrubber temperature at  $42^\circ \pm 1^\circ$ , but this adds a complicating factor to the scrubber design. Moreover, whilst heated scrubbing solutions have been recommended,<sup>1,6,28</sup> Colson<sup>21</sup> has pointed out that the increased possibility of hydrolysis of methyl iodide may lead to low results. As shown in Table II, the negative error was dependent on the volume of water used, and large errors were introduced when sulphur was present (*cf.* the results obtained with water saturated with hydrogen sulphide).

(b) *In presence of 3–4 mg of added sodium sulphate* (equivalent to 1 sulphur atom per methoxy group for 3 mg samples of vanillin) only sodium acetate and sodium bicarbonate of the solutions tested were clearly unsatisfactory (*cf.* ref. 25).

(c) *In presence of larger amounts of sulphur*, both sodium antimonyl tartrate and the sodium thiosulphate + cadmium sulphate mixture began to give low results. This finding explains the differing opinions expressed regarding their efficiency (*cf.* 7 and 25, 8, 10 and 27). In agreement with earlier investigators,<sup>23,29</sup> cadmium sulphate gave good results; it was the only satisfactory solution when a large excess of sulphur was present. The formation of heavy cadmium sulphide precipitates did not influence its efficiency, as has been suggested.<sup>30</sup>

TABLE II. EFFICIENCY OF SOME SCRUBBING SOLUTIONS\* IN METHOXYL DETERMINATIONS IN THE PRESENCE AND ABSENCE OF SULPHUR

Range of weight of vanillin, 2.92–3.39 mg, ∴ methoxyl present approx 0.2 mEquivs.

Composition of scrubbing liquid†		Wt. of sodium sulphate added, mg	∴ Sulphur present, mEquivs	Range of methoxyl recovery, %
5% aq. sodium bicarbonate		0	0	99.4–100.4
		3	0.2	95.1–95.3
		10	0.7	92.5–92.7
		27	1.9	90.0–90.4
25% aq. sodium acetate		0	0	100.0–100.5
		4	0.3	98.1–98.5
		30	2.1	91.1–91.2
10% aq. sodium antimonyl tartrate		0	0	99.5–100.2
		3	0.2	99.6–100.0
		10	0.7	95.1–95.3
		15	1.0	94.1–94.2
5% aq. sodium thiosulphate + 5% aq. cadmium sulphate (1 + 1 V/V)		0	0	100.0–100.5
		3	0.2	100.0–100.1
		10	0.7	99.1–99.5
		18	1.3	97.7–98.0
5% aq. cadmium sulphate		0	0	99.8–100.6
		3	0.2	
		10	0.7	
		15	1.0	
		32	2.2	
Water	2 ml	0	0	99.5–99.7
	4 ml	0	0	98.8–99.2
	2 ml	4	0.3	97.5–97.9
	4 ml	4	0.3	96.8–97.1
Water satd. with hydrogen sulphide	2 ml	0	0	95.2
	3 ml	0	0	94.0
	4 ml	0	0	91.3
	5 ml	0	0	90.7

\* Used in the spiral scrubber described in BS1428 : C 1 : 1954. Flow-rate = 6–8 ml per min. Temp. of solutions =  $20^{\circ} \pm 1^{\circ}$ .

† Volume used = 4 ml, unless otherwise stated.

With high concentrations of hydrogen sulphide, the decreased efficiency of sodium antimonyl tartrate may be caused by complex thio-anion formation from the original  $Sb_2S_3$  precipitate, and subsequent interaction between the thio-anion and alkyl iodide.\* For cadmium sulphate the concentration of hydrogen sulphide is apparently not so critical since cadmium sulphide does not form complex sulphides.

In earlier experiments, Gran<sup>30</sup> found a preliminary water scrubber essential (to remove hydrogen iodide vapour), since otherwise the scrubber acidity increased

\* We are grateful to one of the referees for this suggestion.

sufficiently to cause some dissolution of the cadmium sulphide precipitate. This effect, however, resulted from his use of acid more concentrated than the azeotrope. Although the introduction of a water scrubber removed one source of error, another was simultaneously introduced, as already described; Gran found that this in turn could be minimised by increasing the flow-rate to 40 ml per min. Experiments at this very high flow-rate revealed that the absorption of hydrogen sulphide by water is indeed much less than at 6–8 ml per min; the high flow-rate either decreases the efficiency of scrubbing, or creates a superior competitive “degassing” effect.

In solutions containing sodium thiosulphate + cadmium sulphate, complexing of thiosulphate ions by cadmium will undoubtedly occur. The decreased efficiency of this scrubbing mixture at high sulphur concentrations (at which cadmium sulphate itself remains efficient) is probably due to removal from solution of cadmium as cadmium sulphide. Some of the previously complexed thiosulphate is therefore liberated, so increasing its possibility of reaction with alkyl iodide.<sup>26,27</sup>

Many other aqueous scrubbers have been proposed, *e.g.* red phosphorus suspensions,<sup>1,2,4,28</sup> solutions of organic compounds,<sup>27</sup> acetic acid<sup>8</sup> and hydrochloric acid.<sup>25</sup> The efficiency of these was not investigated.

The B.S. design spiral scrubber gives adequate scrubbing efficiency under the experimental conditions described, but not at greatly increased flow-rates. When aqueous cadmium sulphate was used in two spiral scrubbers joined in series, no detectable leakage of hydrogen sulphide to the second scrubber occurred at a flow-rate of 10 ml per min; slight leakage occurred at 15–20 ml per min. This supports the earlier warning by Heron *et al.*<sup>10</sup> regarding scrubbing efficiency.

#### 6. The use of a solid scrubber

Having established that reaction between hydrogen sulphide and alkyl iodides occurred only in aqueous solution, it appeared that the use of a suitable solid scrubber would eliminate several possible sources of error. The use of solid scrubbers was apparently first suggested by Fierz-David *et al.*,<sup>31</sup> but their use in alkoxy determination attracted little attention until recently.<sup>13,32,33,34</sup>

We have found soda-asbestos (M.A.R.) to be a very efficient solid scrubber, although Vecěra and Spěvák<sup>34</sup> apparently rejected it after trial experiments. It quantitatively absorbs and firmly retains hydrogen iodide, iodine, hydrogen sulphide

TABLE III. EFFICIENCY OF A SODA-ASBESTOS SOLID SCRUBBER

Flow-rate = 6–8 ml/min

Compound	Range of weights taken, mg	∴ Alkoxy present, <i>mEquivs</i>	Wt. of sodium sulphate added, mg	∴ Sulphur present, <i>mEquivs</i>	Range of alkoxy recovery, %
Vanillin	2.736–3.01	approx. 0.2	0	0	99.6–100.5
			10	0.7	99.7–100.5
			30	2.1	99.7–100.5
			60	4.2	99.7–100.1
Phenacetin	2.98–3.61	approx. 0.2	0	0	99.5–100.4
			30	2.1	99.8–100.6
			60	4.2	100.0–100.6

and carbon dioxide; even when quantities of these vapours have been absorbed there is no retention of alkyl iodides. Table III shows its high efficiency under testing conditions. In addition, when 40 mg of sodium sulphate was refluxed for 3 hr, using a flow-rate of 40 ml per min, no hydrogen sulphide passed the scrubber.

Experimentally, the use of a solid scrubber simplifies the apparatus and procedure. The use of nitrogen as flow-gas is, of course, essential. The spiral liquid scrubber is replaced by a straight connecting tube, as shown in Fig. 1; a packing of soda-asbestos 2 inches long is adequate, and is renewed for each analysis.

The reaction conditions described in this paper and the results presented on scrubbers are totally applicable to alkoxy determinations in which the standard gravimetric or iodometric finish is employed.

Details of the investigation of reaction conditions for determination of propoxyl and butoxyl groups, of the differentiation of ester from ether groups, and of the infra-red method for analysis of compounds containing methoxyl and ethoxyl groups will be given shortly in further parts of this series.

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*Zusammenfassung*—Eine empfindliche Infrarotmethode zur quantitativen Bestimmung von Dämpfen wurde verwendet um die Reaktionsvariablen der Alkoxybestimmung nach Zeisel zu studieren. Verschiedene Widersprüche in der Literatur wurden klargestellt. Die Reaktionsbedingungen zur raschen Erzielung genauer Resultate bei der Analyse von festen Körpern und verdampfbaren Flüssigkeiten, selbst in Gegenwart grosser Mengen an Schwefel, werden beschrieben. Es wurde gefunden, dass die Reaktion zwischen Alkyljodid und Schwefelwasserstoff nur in wässriger Lösung stattfindet; die Anwendung von Soda-Asbest als festes Absorptionsmittel hat daher fundamentalen Vorteil gegenüber einer wässrigen Lösung und gibt exzellente Resultate. Mit Vanillin ausgeführte Testbestimmungen zeigen eine Standardabweichung von 0.16%.

*Résumé*—Une méthode infra-rouge sensible pour la détermination quantitative des vapeurs a été utilisée pour l'étude des variables de la réaction dans le dosage des alkoxy de Zeisel. Différents rapports contradictoires dans la littérature ont été clarifiés. Les conditions de réaction, donnant des dosages rapides et précis pour des solides et des liquides volatils, même en présence d'une grande concentration de soufre, sont décrites; pour des dosages de vanilline, l'écart standard est 0,16%. Les auteurs ont trouvé que l'interaction entre les iodures d'alkyl et l'hydrogène sulfuré se produisait seulement en solutions aqueuses; l'utilisation d'amianté sodée comme laveur solide a cependant des avantages fondamentaux sur les solutions aqueuses, et donne d'excellents résultats.

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# APPLICATIONS OF INFRARED SPECTROSCOPY—III\*

## THE SIMULTANEOUS DETERMINATION OF METHOXYL AND ETHOXYL GROUPS

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**Summary**—Quantitative vapour-phase infrared spectroscopy permits the simultaneous determination of methoxyl and ethoxyl groups as alkyl iodides or bromides: when the methoxyl/ethoxyl ratio exceeds 4 : 1, determinations are only possible as bromides. The reaction-time involved is 30 min. Results, correct to within  $\pm 1\%$  for each alkoxy group, can be obtained on the micro-scale. The presence of sulphur does not interfere.

PART II<sup>1</sup> of this series described a spectroscopic investigation of some of the reaction variables of the Zeisel determination, and results were reported for micro alkoxy determinations on reference compounds. These showed that the spectroscopic method of determining the liberated alkyl iodides not only gave results comparable in accuracy and reproducibility with those obtainable by the more conventional methods, but also distinguished in the same analysis between different alkoxy groups. On unknown compounds, this selective information cannot be obtained directly if the conventional iodometric or gravimetric finishes are used.<sup>2,3</sup>

Gran<sup>2</sup> reviewed the techniques available for the simultaneous determination of methoxyl and ethoxyl groups; the majority require time-consuming modification or extension to the standard Zeisel method. Techniques based on Martin and Vertalier's<sup>4</sup> use of gas chromatography were later introduced<sup>5,6</sup> which, although not comparable in accuracy with the more conventional methods, offered possibilities for future development. More recent publications, however, have merely reverted to modifying<sup>7</sup> the Willstätter and Utzinger<sup>8</sup> technique or to describing modifications<sup>9,10</sup> of the combustion method.<sup>11</sup>

This paper describes how the quantitative infrared technique<sup>1,12</sup> can be extended, without modification or loss in accuracy, to the simultaneous determination of both methoxyl and ethoxyl groups. Results, correct to within  $\pm 1\%$  for both groups, can be obtained on the microscale. The reaction-time is 30 min, and only one weighing of the sample is involved. The presence of excess sulphur (which continues to cause difficulty<sup>13</sup>) in any form or quantity does not interfere.

### EXPERIMENTAL

#### *Gas-cells*

Descriptions of the gas-cells used, and data giving their useful concentration range and sensitivity have been given.<sup>1,12,14</sup>

\* Part II—see ref. 1.

### Spectrometer

The spectrometer used was a Hilger H800 double-beam instrument, which has the following advantages: (a) accommodation of gas-cells up to 56 cm long, (b) linear recording of percentage absorption, with an accuracy of  $\pm 0.5\%$ . This fixes the limiting accuracy of the method, and obviates the necessity of weighing 2-5 mg samples to the nearest microgram. (By adjustment of tares, all weighings were made within the range of the 0-30 mg gradicule scale of an aperiodic direct-reading balance having an accuracy of  $\pm 10 \mu\text{g}$ .)

### Spectrometer conditions

For the calibration curve to be of maximum accuracy, the standard operating conditions (slit-width, scan speed, electronic gain etc.) must be carefully selected initially and subsequently rigorously controlled during determinations. The gas-cell carrier must be rigidly fixed, or fitted with some simple

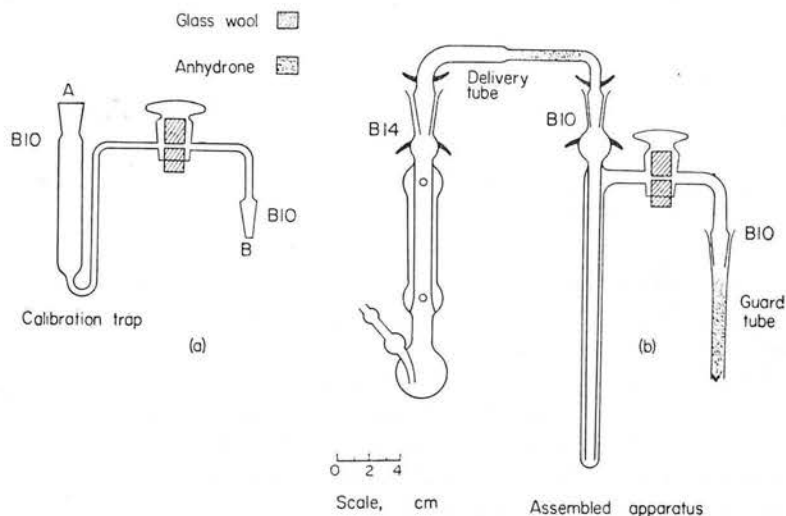


FIG. 1.—(a) Calibration trap. (b) Assembled apparatus.

locating device ensuring replacement each time in identical position with respect to the infrared beams.

Reproducibility of percentage absorption for a given concentration depends on the recorder zero-stability; any peak height must always be measured with respect to some arbitrarily fixed base-line or zero associated with the wave-length involved. All other conditions being constant, the base-line may be affected by small energy losses caused by fogged or scratched cell-windows, which must therefore be kept in good condition. Small local variations in base-line caused by such factors may, however, be satisfactorily compensated by adjustment of some auxiliary compensating device interposed in the reference beam.

### Construction of calibration curves

Weigh the required amount of alkyl iodide in a micro weighing-bottle ( $12 \times 4 \text{ mm}$ ) fitted with a leak-proof ground-glass stopper. Via *A*, place the bottle in the trap shown in Fig. 1(a), then immerse the limb of the trap in liquid nitrogen. Insert the requisite evacuated gas-cells at *A*, connect *B* to a suitable vacuum-line,<sup>12</sup> and evacuate the system with the trap still in coolant.

Vaporise the trapped alkyl iodide into the gas-cell, making the total pressure equal to atmospheric, by the technique already described.<sup>12</sup> Quantitative transfer, within the experimental limits of  $\pm 1\%$ , is easily achieved. Record the particular absorption peak selected for calibration (see below) six times, then calculate the mean peak height: this minimises any error in the peak heights drawn by the pen recorder, the reproducibility of which is  $\pm 0.25\%$ .

Fundamentally, peak areas are proportional to concentration, but at the partial pressures used

peak heights are sensitive to concentration changes and are, under standard conditions, much easier to measure. "Pressure-broadening" effects do not cause complications.<sup>12</sup> Consequently, calibration curves can be constructed with reference to peak heights. Fig. 2 shows typical curves obtained.

#### Efficiency of trapping

Various weights of alkyl iodides were added to the reaction-flask and volatilised using flow-rates between 4 and 20 ml per min. At each flow-rate, recoveries ranged from 99.0–101.0% with an equal distribution of high and low results. In several experiments, two absorption traps were connected in series: in no case was alkyl iodide detectable in the second trap. These experiments led to  $\pm 1\%$

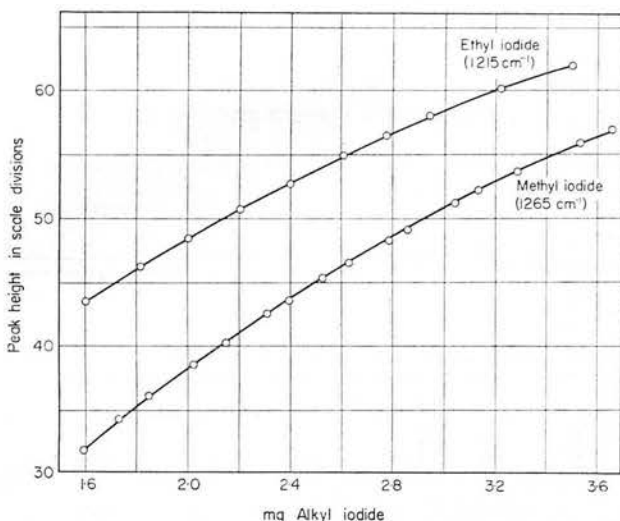


FIG. 2.—Calibration curves for methyl iodide and ethyl iodide.

being claimed as the accuracy of the method. In practice, results better than these limits can be expected (see Table I).

#### Alkoxy determinations

Details of the apparatus, reagents, flow-gas, heating, reaction-time, and weighing of samples have been described.<sup>1</sup> For volatile samples, the described technique obviating use of double distillation<sup>1</sup> is used; it may also be applied to non-volatile and solid samples. The following technique, however, has been successfully used for solids: weigh the sample in a long-handled weighing spoon.<sup>1</sup> Add 20–40 mg phenol to the spoon, and warm *gently* over a hot-plate to form a homogeneous melt at as low a temperature as possible. Place the spoon in a reaction-flask to which 6 ml of hydriodic acid had been added, pre-conditioned as described,<sup>1</sup> and cooled.

#### Procedure

Attach the delivery tube (Fig. 1(b)), packed with fresh Anhydrone, to a clean trap fitted with an Anhydrone guard-tube: immerse the trap in liquid nitrogen. (This order of assembly minimises collection of atmospheric water-vapour in the trap.) Attach the B14 cone of the delivery tube to the reaction condenser, so assembling the apparatus as shown in Fig. 1(b). Adjust the nitrogen flow-rate to 6–8 ml per min, and begin heating the reaction-flask.

After 30 min reflux, remove and stopper the trap, keeping it immersed in coolant. When convenient, volatilise the trapped reaction products into the appropriate gas-cell. Draw the spectrum of the products—this reveals immediately which iodides are present. Then re-draw 6 times (ensuring that the correct base-line is given) the characteristic peak on which calibration of each iodide is based. Refer the average peak height for each iodide to the appropriate calibration curve, and hence determine the weight of alkyl iodides liberated.

## RESULTS

*Interferences*

Since iodine, hydrogen sulphide and hydrogen iodide vapours do not interfere with the spectroscopic determination, conventional Zeisel scrubbers are not necessary. Phosphine, however, does interfere; preconditioning of the hydriodic acid as described<sup>1</sup> is required, and subsequent addition of hypophosphites to decolourise dark reaction mixtures should be avoided. The use of colourless hydriodic acid is not necessary for quantitative results. Since water vapour must be excluded in spectroscopic determinations, the reaction products are trapped after passage through Anhydrone<sup>1</sup>.

*Choice of calibration peaks*

Fig. 3 diagrammatically represents the spectra given in the 800–1500  $\text{cm}^{-1}$  region,

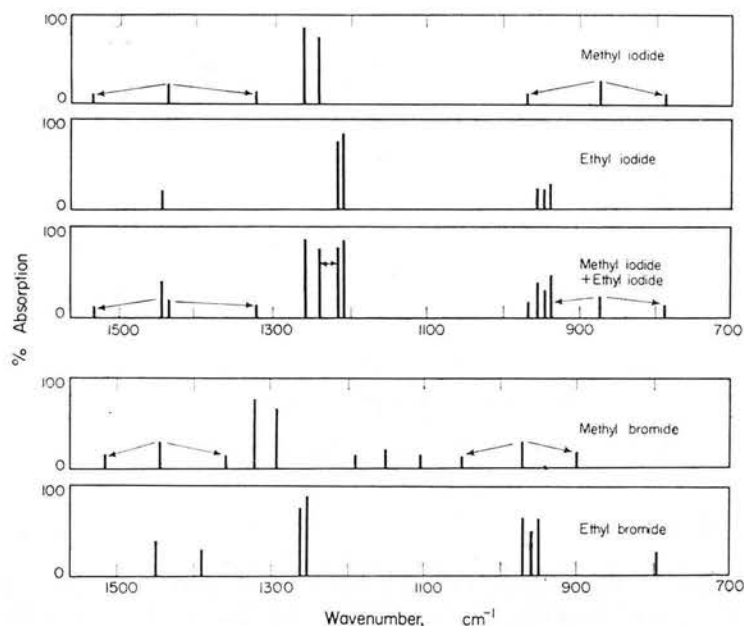


FIG. 3.—Representation of spectra given by methyl iodide, ethyl iodide, methyl bromide and ethyl bromide.

at a scan speed of 127  $\text{cm}^{-1}$  per min, by methyl iodide, ethyl iodide, and by a mixture of the two. If a vapour contains only one component, calibration can be based on any convenient absorption peak in the spectrum, although maximum sensitivity and accuracy will clearly be obtained if calibration is based on the most intense absorption. In mixtures, however, over-lapping or coincidence of peaks can occur. Calibration for a particular component must then be based on the most intense absorption which is not masked or reinforced by peaks given by the other components present.

In the composite spectrum (Fig. 3) given by a mixture of methyl + ethyl iodides, very slight overlapping of peaks occurs at the normal scanning speed, so that the 1244  $\text{cm}^{-1}$  peak of methyl iodide fractionally increases the height of the 1215  $\text{cm}^{-1}$  ethyl iodide peak. The 1265  $\text{cm}^{-1}$  methyl iodide peak is not masked, and so calibrations based on it give correct methoxyl values as shown by the typical results given in Table I.

Calibrations based on the 1215  $\text{cm}^{-1}$  ethyl iodide peak, however, lead in this circumstance to high ethoxyl values: the more minor peaks given by ethyl iodide at 1450  $\text{cm}^{-1}$  and 950  $\text{cm}^{-1}$  are also subject to overlapping with minor methyl iodide peaks and so cannot be used.

Fortunately, this positive ethoxyl error was found to be a linear function of the

TABLE I. SIMULTANEOUS METHOXYL/ETHOXYL DETERMINATIONS

Compound or mixture	Weight taken, mg	Wt. alkyl iodide found		Corr. wt. $\bar{\text{EtI}}$ found,* mg	Methoxyl		Ethoxyl	
		$\bar{\text{MeI}}$ , mg	$\bar{\text{EtI}}$ , mg		found, %	theory, %	found, %	theory, %
Vanillin   Phenacetin	7.41 3.29	6.94	3.00	2.86	20.4	20.4	25.2	25.1
Vanillin   Phenacetin	10.24 3.02	9.52	2.82	2.63	20.3	20.4	25.3	25.1
Vanillin   Phenacetin	2.03 4.28	1.90	3.75	3.71	20.5	20.4	25.1	25.1
Anisic acid   Cmpd X†	9.43 7.20	8.72	3.15	2.98	20.2	20.4	12.0	12.0
Cmpd Y†   	2.60	6.26	2.40	2.28	52.7	52.3	25.8	25.3
Cmpd Z†   	1.42	0.98	3.22	3.20	15.1	15.0	65.1	65.5

\* Corrected weight  $\bar{\text{EtI}} = (\text{wt. } \bar{\text{EtI}} \text{ found}) - (0.019)(\text{wt. } \bar{\text{MeI}} \text{ found})$ .

† Origin of samples:

Cmpd X: 4-chloro-2-ethoxy-p-tosyl-1-naphthylamine (Prof. F. Bell)

Cmpd Y: 1:1:3-trimethoxy-3-ethoxypropane

Cmpd Z: 1:1:3-triethoxy-3-methoxypropane } L. Light and Co. Ltd. (redistilled).

weight of methyl iodide present, and a correction factor (0.019), applicable to a particular set of standard spectrometer conditions, was calculable. When

$$(0.019) \times (\text{weight of methyl iodide found})$$

was subtracted from the actual weight of ethyl iodide found, the results shown in Table I were obtained for methoxyl-ethoxyl compounds or for synthetic mixtures ranging in composition from methoxyl/ethoxyl = 3:1 to 1:3.

At low ethoxyl contents, the 1215  $\text{cm}^{-1}$  ethyl iodide absorption occurs as a shoulder on the 1244  $\text{cm}^{-1}$  methyl iodide peak and determinations become inaccurate: at methoxyl/ethoxyl ratios  $> 4:1$ , there is no measurable ethyl iodide peak height and the method fails. Although such combinations must be rare in actual chemical compounds, they could readily be met in determinations on mixtures of methoxyl and ethoxyl compounds. Such mixtures can be analysed by using hydrobromic acid in place of hydriodic acid during reflux.

*Alkoxy determinations using hydrobromic acid*

Constant-boiling hydrobromic acid (sp. gr. 1.47) is effective in cleaving alkoxy groups: it produces alkyl bromides quantitatively from esters and ethers almost as quickly (15–20 min for methyl and ethyl) as hydriodic acid forms the corresponding iodides. Alkyl bromides are as conveniently estimated as alkyl iodides by the infrared technique if the required calibration curves are constructed (the manometric technique<sup>12</sup> must be used for methyl bromide, b.p. 3.6°). Moreover, Fig. 3 shows that the 1320 cm<sup>-1</sup> absorption of methyl bromide is so widely separated from the 1250 cm<sup>-1</sup> peak of ethyl bromide that calibrations based on each of these are valid for the analysis of all possible methoxyl/ethoxyl percentage compositions. The only slight disadvantage in the use of the bromides is a small decrease in sensitivity. Gas-cell "B"<sup>14</sup> permits determination of approximately 2–6 mg of alkyl bromide as opposed to 1–4 mg of alkyl iodide; this requires that sample weights of alkoxy compounds must be approximately doubled when determination as the bromide is used. Results equal in accuracy to those shown in Table I are, however, obtainable without the necessity of using a correction factor.

## CONCLUSIONS

The method described permits satisfactory simultaneous determinations of methoxyl and ethoxyl groups on the micro scale. Although Table I shows only a few typical results, many determinations have been made during the past 18 months on a wide range of polyfunctional compounds, each of which contained, in addition to alkoxy, one or more of the following groups: —F, —Cl, —Br, —I, —NO, —NO<sub>2</sub>, —NH<sub>2</sub>, =NH, —N=N—, =S, —SO<sub>3</sub>H, ≡PO<sub>4</sub>, —PS, =Se. Satisfactory results were obtained on pure samples; in our experience, some organic compounds are surprisingly difficult to purify sufficiently for satisfactory results to be obtained in the alkoxy determination, which is a rigorous functional group analysis.

The accuracy obtainable, small samples required, short reaction time, elimination of conventional scrubbers, and absence of interference from sulphur combine to make this spectroscopic method undoubtedly superior to any method previously described for simultaneous determination of alkoxy groups. At the present time, when ever-increasing numbers of chemists have access to an infrared spectrometer, this method should be of general interest.

*Acknowledgements*—We thank Professor E. L. Hirst, C.B.E., F.R.S., for his interest in this work, and the Carnegie Trust for the award of a Scholarship (to J. L. D.).

**Zusammenfassung**—Quantitative Infrarotspektroskopie in der Gasphase erlaubt die gleichzeitige Bestimmung von Methoxyl- und Äthoxylgruppen als Alkalijodide oder Bromide. Wenn das Verhältnis Methoxyl:Äthoxyl den Betrag von 4:1 überschreitet kann die Bestimmung nur über die Bromide durchgeführt werden. Die benötigte Reaktionszeit ist 30 Minuten. Die Resultate, innhalb von ±1% genau, können für Proben im Mikrobereich erhalten werden. Gegenwart von Schwefel stört nicht.

**Résumé**—La spectroscopie infra-rouge quantitative en phase vapeur permet le dosage simultané des groupements méthoxy et éthoxy à l'état d'iodures ou de bromures d'alkyl: quand le rapport méthoxy/éthoxy dépasse 4/1, les dosages ne sont possibles que pour les bromures. Le temps de réaction nécessaire est de 30 minutes. Les résultats, corrects dans l'intervalle de ±1 pour cent pour chaque groupement alkoxy, peuvent être obtenus à l'échelle microscopique. La présence de soufre ne gêne pas.

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## APPLICATIONS OF INFRARED SPECTROSCOPY—IV\*

### THE CAUSES OF ANOMALOUS ALKOXYL DETERMINATIONS GIVEN BY SUGARS AND POLYHYDRIC ALCOHOLS

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**Summary**—The volatile reaction products from Zeisel determinations on sugars and related compounds have been identified. One of the products from certain common sugars is 2,5 dimethylfuran, which interferes with the Vieböck iodometric determination of alkyl iodide, and has been shown to be a contributing cause of apparent alkoxy values. Suggestions that hexyl iodide is evolved from sugars and that vinyl iodide is a product from polyhydric alcohols have been disproved.

ZEISEL determinations on unmethylated sugars and polysaccharides have been reported<sup>1,2</sup> to give small apparent alkoxy values. This implied that all carbohydrate materials would give slightly high analytical results, and made particularly difficult the interpretation of analyses of polysaccharide functions having a small but real methoxy content.

In contrast, Goldstein and Smith<sup>3</sup> found that certain periodate oxidation products gave very high results. They proposed that the liberation of "extra" alkyl iodide from polyhydric alcohols such as glycerol was responsible. Von Rudloff<sup>4</sup> had earlier reported that polyhydric alcohols gave anomalous alkoxy values. Strangely, he also obtained very unsatisfactory results for  $\alpha$ -methyl-D-glucoside, a recommended reference standard<sup>5</sup> which gives excellent results.<sup>6-9</sup> Although it had been clearly established that the volatile products from ethylene glycol were ethylene + ethyl iodide, von Rudloff claimed that vinyl iodide + ethyl iodide were formed.

It is significant that the apparent methoxy values quoted for standard compounds *e.g.* glucose and sucrose, ranged from zero to 0.4% (*cf.* refs. 1 and 2). Modification of Willstätter and Utzinger's trimethylamine technique<sup>11</sup> was found<sup>1-3</sup> to give results more satisfactory (although still high) than were obtained by the more convenient Vieböck iodometric titration. Recently, in a paper<sup>13</sup> which apparently repeats the published description<sup>14</sup> of a combustion method for alkoxy determinations, Fukuda states that the method is not applicable to carbohydrates or related substances; the combustion method fails, in fact, for compounds liberating any non-acidic organic vapour in addition to alkyl iodides.

The identity of the volatile products from carbohydrate materials, and the sources of error contributing to the anomalous results, have hitherto not been clearly established. For simple sugars, Gran<sup>2</sup> showed that the apparent methoxy content was not caused by traces of contaminating alcohols *etc.* He suggested that the formation of volatile hexyl iodides was responsible, although he could not identify or isolate such products.

\* Part III—D. M. W. Anderson and J. L. Duncan, *Talanta*, 1961, 8, 1.

The proposals of von Rudloff and Gran were clearly based on inadequate experimental evidence: further investigation was desirable. Following our studies<sup>9,15</sup> of certain aspects of the Zeisel determination, it appeared that vapour-phase infrared spectroscopy could be applied to identify the volatile products from sugars and related compounds.

## EXPERIMENTAL

### *Apparatus*

The reagents, reaction conditions, and apparatus used for alkoxy determinations were as described.<sup>9</sup> The technique for trapping volatile products, and details of the infrared method for their subsequent identification, have been given.<sup>16,17</sup>

### *Reagents*

Glucose, sucrose, mannitol—all M.A.R.

5-Hydroxymethylfurfural was prepared by Haworth's method.<sup>18</sup>

5-Methylfurfural, furan, 2-methylfuran, 2,5-dimethylfuran and compounds not described in footnotes to Table I were commercial samples which conformed, after purification where necessary, to literature description.

### *Procedure*

Samples (30–60 mg) of the compounds listed in Tables I and II were refluxed for 1 hr with hydriodic acid (6 ml, constant-boiling, pre-conditioned<sup>9</sup>) using nitrogen as flow-gas (6–8 ml per min.). The mixture of volatile products was collected, after passage through Anhydrone, in a trap immersed in liquid nitrogen. The components of each mixture were subsequently identified and quantitatively determined by vapour-phase spectroscopy<sup>16,17</sup>: since 2-iodohexane (b.p. 165°) was insufficiently volatile, it was identified as a pure liquid. All components were identified without difficulty; none of the mixtures was sufficiently complex for prior separation of the components by vapour-phase chromatography to be necessary.

## RESULTS

Table I shows the products liberated in 1 hr from 30-mg to 60-mg samples of sugars and polysaccharide materials. The products from polyhydric alcohols are shown in Table II.

### *Effect of varying reaction-time and sample weights*

The results obtained from experiments with glucose are shown in Table III.

### *Volatilisation of iodine*

With 60 mg of glucose, only small amounts of iodine were released, insufficient to form a sublimate on the condenser walls: iodine did not pass the condenser. With 250-mg and 500-mg samples, however, extensive volatilisation occurred.<sup>9</sup> Although most of this condensed, some iodine reached the cold trap in which the volatile products were collected. The efficiency of removal of such quantities of iodine by 10% aq. sodium antimony tartrate in the B.S. design of scrubber<sup>9</sup> was therefore tested. When 100 mg of iodine were refluxed with pre-conditioned hydriodic acid, the amount of iodine passing the scrubber increased the reagent blank from 0.03 ml of 0.01N sodium thiosulphate to 0.06 ml (*cf.* ref. 8). When 500 mg of glucose was refluxed, the apparent methoxyl content found iodometrically was exactly equivalent to the amount of methyl iodide found by the infrared method in a duplicate run.

TABLE I

Compound*	Yield of volatile products†‡					
	n-Heptane	n-Hexane	n-Pentane	n-Butane	2,5 Dimethyl-furan	Acetone
Glucoheptose	tr	—	—	—	—	—
2-Deoxyglucose	—	tr	—	—	—	—
5-Hydroxymethylfurfural	—	tr	—	—	—	—
Glucose, hexoses	—	tr	—	—	2%	—
Fructose, sorbose	—	1%	—	—	2%	—
Rhamnose, fucose	—	1%	—	—	2%	—
Glucosamine HCl	—	tr	—	—	tr	tr
Sucrose	—	tr	—	—	2%	1%
Glucurone <sup>a</sup>	—	—	tr	—	—	—
Xylose, pentoses	—	—	tr	—	—	—
Furfural	—	—	tr	—	—	—
5-Ketogluconolactone <sup>b</sup>	—	—	tr	—	—	tr
Galactono- $\gamma$ -lactone <sup>c</sup>	—	—	tr	—	—	tr
Erythrose	—	—	—	tr	—	1%
Glyceraldehyde	—	—	—	—	—	1%
Oat starch <sup>d</sup>	—	tr	—	—	1%	—
Waxy maize starch	—	tr	—	—	3%	tr
Glycogen <sup>e</sup>	—	tr	—	—	3.5%	tr
Inulin <sup>f</sup>	—	tr	—	—	4.5%	tr
Agar <sup>f</sup>	—	tr	—	—	2%	tr
Cellulose <sup>g</sup>	—	—	—	—	2%	tr
Araboxylan <sup>h</sup>	—	—	tr	—	—	—

\* 30–60 mg in 6 ml of HI under reflux for 1 hr.

† expressed as % of wt. of sample taken; tr denotes  $\geq 0.02\%$ .

‡ In addition to the products shown, all compounds in this table gave a trace of CO<sub>2</sub>, except for a, b and c, which gave approx. 0.75 mole of CO<sub>2</sub> per mole of compound.

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f, B.D.H. Ltd.

g, ex *Nitella translucens*; Anderson and King, in preparation.

h, ex Rye flour; Aspinnall and Sturgeon, *J. Chem. Soc.*, 1957, 4469.

TABLE II

Compound*	Volatile products†
Sorbitol, mannitol	CO <sub>2</sub> (tr) + n-hexane (tr) + 2-iodohexane
Ribitol	CO <sub>2</sub> (tr) + n-pentane (tr) + 2-iodopentane
Erythritol	CO <sub>2</sub> (tr) + 2-iodobutane
Glycerol	isopropyl iodide
Ethylene glycol	ethylene + ethyl iodide
Allyl alcohol	isopropyl iodide
Vinyl ethyl ether	ethyl iodide

\* Reaction details as in Table I, footnote †.

† For yields of alkyl iodides, see Discussion: tr denotes  $\geq 0.02\%$ .

## DISCUSSION

When a carbohydrate material is suspected to have a low methoxyl content, large sample weights must be employed if the methyl iodide released is to be determined accurately. There is also a tendency for reflux periods longer than normal to be used (*cf.* ref. 2). Table III shows that *up to a certain ratio* (100 mg of sample per 6 ml of hydriodic acid) the volatile products from sugars are independent of the sample weight taken: for larger samples, different decomposition mechanisms are clearly

TABLE III

Wt. of glucose, mg*	Reflux period, hr	Volatile products†
20-100	1	CO <sub>2</sub> (tr) + n-hexane (tr) + 2,5-dimethylfuran (2%)
20-100	4	CO <sub>2</sub> (tr) + n-hexane (tr) + 2,5-dimethylfuran (4%)
250	1	CO <sub>2</sub> (tr)
500	1	CO <sub>2</sub> (tr) + methyl iodide (0.12%)
500	3	CO <sub>2</sub> (tr) + methyl iodide (0.4%)

\* treated with 6 ml of HI under reflux.

† yields expressed as in Table 1.

involved. Hexyl or other iodides are only liberated, however, when hexahydric alcohols are present. This, therefore, refutes the suggestion made by Gran.<sup>2</sup> Table III shows that methyl iodide is only formed when exceptionally large weights of sugars are reacted; the very small amount liberated (equivalent to 0.03% and 0.1% of methoxyl after 1 and 3 hours respectively) does not explain in full the anomalous results previously reported.

Alternative possible sources of error were therefore investigated. Those included (a) volatilisation of iodine, (b) formation of 2,5-dimethylfuran and of hydrocarbons and acetone, (c) retention by polysaccharides of organic solvents used in their preparation.

*Volatilisation of iodine*

Previous workers<sup>7,8</sup> have commented on the volatilisation of small but significant quantities of iodine. In particular, Belcher<sup>8</sup> showed that volatilisation could occur, although correct results were obtainable if the appropriate increased "blank" value was taken into account. This, however, indicates that iodine vapour, when liberated in quantity, is not *totally* retained by aqueous scrubbers. Our results are in agreement, but the amounts of iodine passing the scrubber are very small, even under testing conditions.

Volatilisation of iodine is therefore not the only possible source of error, although it may well have made a major contribution to some of the high results reported by previous workers, particularly when very large sample weights, fast flow rates and long reflux periods were used. Any tendency for errors to arise through volatilisation of iodine can be minimised by use of the solid scrubber, soda-asbestos.<sup>19</sup>

*Result of formation of 2,5-dimethylfuran*

The observation that 2,5-dimethylfuran is one of the volatile reaction products from certain sugars permits a new explanation of anomalous high results to be given. Soda-asbestos and the scrubbing solutions normally used in the Zeisel determination do not absorb 2,5-dimethylfuran.

When 100 mg of this compound were added to 10 ml of the conventional oxidising solution (glacial acetic acid/bromine/potassium acetate) used in the iodometric determination of alkyl iodides,<sup>12</sup> a reaction, clearly involving bromine, took place. A precipitate, found to be potassium bromide, was produced. When the determination was completed in the usual way, the thiosulphate titre indicated, when carried out immediately, an apparent addition of 0.9 mg of methyl iodide. If 10 min were allowed to elapse before titrating,<sup>6</sup> the titre was equivalent to 1.8 mg of methyl iodide, indicating 0.4% of methoxyl. Slow liberation of iodine continued for 5 hours, when the apparent methoxyl content was 1.2%. Furan and 2-methylfuran reacted similarly, but liberated smaller quantities of iodine than 2,5-dimethylfuran. The effect of 2,5-dimethylfuran

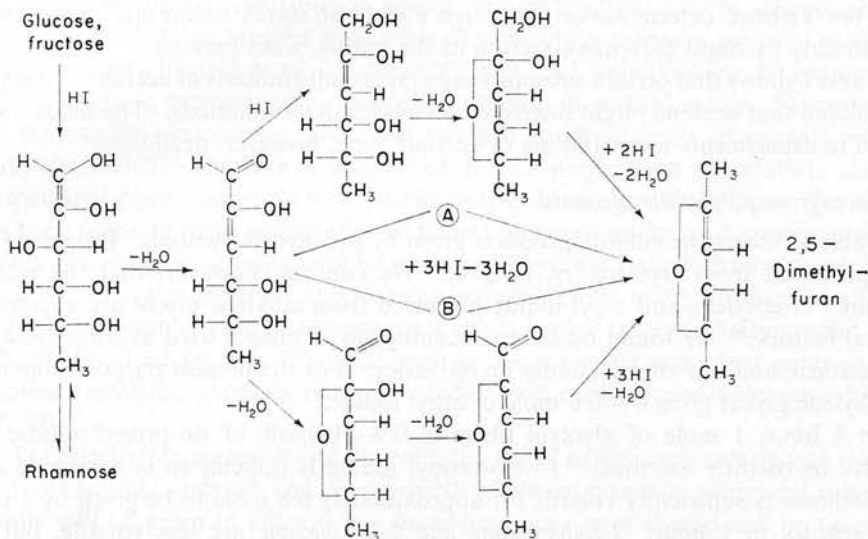


FIG. 1.

was not associated with addition of excess formic acid<sup>20</sup> or excess sodium acetate and sulphuric acid,<sup>21</sup> and clearly contributes to the anomalous Zeisel reactions of sugars.

When furan is added to a cold solution of bromine in acetic acid containing potassium acetate, potassium bromide is precipitated and 2,5-diacetoxy-2,5-dihydrofuran, which is hydrolysed to malealdehyde, is produced in good yield.<sup>22</sup> Our experiments show that both 2-methyl- and 2,5-dimethylfuran react analogously to furan, although 2,5-diacetoxy-2-methyl-5-hydrofuran was too unstable<sup>23,24</sup> to be isolated from the 2-methylfuran reaction mixture. The following facts suggest that the hydrolysis products are involved in the liberation of titratable iodine: (a) iodine is released continuously for 4–5 hour, (b) the relative instabilities of the diacetoxy addition products increase in the order, furan, 2-methylfuran, 2,5-dimethylfuran, which is the order of increasing yields of iodine by these substances.

Pathway *A* in Fig. 1 shows a possible reaction mechanism for the unexpected formation of 2,5-dimethylfuran. When 5-methylfurfural was refluxed with hydriodic acid, extensive resinification and polymer formation occurred; negligible amounts of 2,5-dimethylfuran were produced. Pathway *B* is therefore not operative. From Tables I and II, it is also apparent that reaction of glucose with hydriodic acid does not involve the intermediate formation of sorbitol.

Quantitative infrared experiments showed that 100 mg of glucose refluxed with hydriodic acid (6 ml) for 1 hour liberated 2 mg of 2,5-dimethylfuran. This, it can be calculated from the results already given, would liberate iodine equivalent to an apparent methoxyl content of 0.01%. The yields of 2,5-dimethylfuran that are found explain positive errors of the magnitude reported by Adams and Castagne,<sup>1</sup> whose results have been duplicated in experiments using the Vieböck titration.

#### *Result of liberation of hydrocarbons and acetone*

The n-hydrocarbons liberated (see Table I) are, like 2,5-dimethylfuran, not retained by the scrubbers normally employed. Pentane, hexane and heptane did not interfere with the Vieböck determination, although a sluggish starch/iodine end-point, caused presumably by slight solvent-extraction of the iodine, was observed.

Table I shows that certain substances liberate small amounts of acetone. Morgan<sup>10</sup> considered that acetone might interfere in Vieböck determinations. The blank values found in experiments using 100 mg of acetone were, however, negligible.

#### *Products from polyhydric alcohols*

Table II shows the volatile products given by polyhydric alcohols. Propylene was not produced from glycerol (*cf.* ref. 10). We confirm, however, that the relative amounts of ethylene and ethyl iodide produced from ethylene glycol are affected by several factors;<sup>10</sup> we found that the concentration of phenol used as solubiliser was also critical, and this effect is under investigation. For the present purpose, one mole of ethylene glycol gives 0.4–0.6 mole of ethyl iodide.

In 1 hour, 1 mole of glycerol liberates 0.9–1.0 mole of iso-propyl iodide. The relative involatility ascribed<sup>7,10</sup> to iso-propyl iodide is difficult to understand; even 2-iodobutane is sufficiently volatile for approximately 0.8 mole to be given by 1 mole of erythritol in 1 hour. 2-Iodopentane and 2-iodohexane are less volatile, but the amounts volatilised in 1 hour indicated apparent methoxyl contents of 40% for ribitol and 15% for mannitol. (*cf.* ref. 4).

#### *Formation of vinyl iodide*

Von Rudloff's proposal that vinyl iodide was formed from ethylene glycol in the Zeisel reaction was not substantiated. Allyl alcohol gives 1 mole of iso-propyl iodide, whilst vinyl ethyl ether gives 1 mole of ethyl iodide as the only volatile product (see Table II). Vinyl propionate gives no volatile products. The reaction



(which represents the essential reaction involved in the standard method<sup>25</sup> for analysis of vinyl ethers) explains our findings. Vinyl groups are converted to acetaldehyde, which immediately polymerises so that no volatile products result. Vinyl iodide is therefore not a possible volatile reaction product in Zeisel determinations.

Von Rudloff's proposal<sup>4</sup> was based on the detection of formaldehyde after passage of the volatile products from the reaction of ethylene glycol with HI (*i.e.*, ethylene and ethyl iodide) through a permanganate-periodate reagent. Tests show that this oxidising reagent produces some formaldehyde from ethylene; there is therefore no need to postulate formation of vinyl iodide in order to explain the production of formaldehyde.

## CONCLUSIONS

It is evident that several factors can contribute to cause anomalous results. Samples should not be larger than required to give the minimal amount of methyl iodide determinable. The reflux period should not be longer than normal; true methoxy compounds react within 8–12 minutes,<sup>7,9,13,26</sup> and it is suggested that reflux of carbohydrate materials for longer than 1 hour leads only to increased error. High results from volatilisation of iodine can be eliminated by using the soda-asbestos scrubber.<sup>9,19</sup> Small positive errors of the magnitude reported by Adams and Castagne<sup>1</sup> are given in the Vieböck procedure; these are caused by the production of 2,5-dimethylfuran.

The larger errors reported by certain authors (*cf.* refs. 1,2) cannot be explained by the 2,5-dimethylfuran contribution alone; two suggestions can be offered. Firstly, that abnormally large samples were allowed to react for excessive periods, so creating errors through liberation of 2,5-dimethylfuran and volatilisation of iodine; and possibly also, in extreme cases, through formation of methyl iodide. Secondly, that the polysaccharide samples concerned retained small amounts of organic solvents, particularly alcohols, ethers or esters used in their preparation or isolation. Jansen<sup>27</sup> warned that pectic materials were particularly liable to give this effect; the warning has been repeated more recently<sup>28</sup> with regard to wood products. Experiments<sup>29</sup> have shown that organic solvents used to de-fat or dehydrate polysaccharide materials are retained, up to temperatures at which the materials begin to decompose, despite oven and high-vacuum drying at temperatures much higher than the boiling-point of the solvents involved (*cf.* ref. 27). Although pectic materials and plant gums gave the greatest retention, starches retained smaller but easily measurable quantities (*cf.* ref. 30).

Polysaccharide materials isolated with the aid of organic solvents should therefore be re-dissolved, dialysed and freeze-dried wherever possible, otherwise misleading results will be given in alkoxy and other analyses: care should still be taken with freeze-dried samples, which can retain solvents.<sup>31</sup> When freeze-drying is not possible, the use of methanol and methoxy compounds should be avoided; analysis by one of the valid methods<sup>15,32</sup> for methoxy in presence of ethoxy can then be used. For materials suspected to contain both methoxy and ethoxy groups, the use of isopropanol or acetone during preparation will allow the infrared method<sup>15</sup> to give the true content of both alkoxy groups: methoxy determinations may also be made in the presence of polyhydric alcohols, since none of these (see Table II) liberate methyl iodide. Indeed, examination of the spectrum of the mixture of volatile reaction products would also reveal which polyhydric alcohols, or mixtures thereof, were present, if this were not otherwise known. Valuable evidence in structural studies, in the detection of anomalous linkages, and in the examination of products obtained by periodate oxidation<sup>3</sup> or hydrogenolysis<sup>33</sup> may thus be given by the infrared method, which also offers a rapid method for "difficult" analyses such as the determination of glycerol in presence of residual sugar substrates and 2,3-butanediol.<sup>34</sup>

*Acknowledgements*—We thank Professor E. L. Hirst, C.B.E., F.R.S., for his interest in this work, and the Carnegie Trust for the award of a Scholarship (to J. L. D.)

*Zusammenfassung*—Die flüchtigen Reaktionsprodukte, die während der Zeiselbestimmung von Zuckern und ähnlichen Substanzen entstehen, wurden identifiziert. Ein Produkt aus gewöhnlichen Zuckern ist 2,5-Dimethylfuran, welches die Bestimmung von Alkyljodid nach Vieböck stört. Es

wurde gezeigt, dass diese Substanz dazu beiträgt, dass scheinbare Alkoxywerte erhalten werden. Die Annahmen, dass Hexyljodid gebildet wird und dass Vinyljodid als Produkte aus Polyalkoholen entstehen, wurde als unzutreffend bewiesen.

**Résumé**—Les produits de réaction volatiles obtenus dans les dosages de sucres et de composés apparentés par la méthode de Zeisel ont été identifiés. Un de ces produits obtenu à partir de certains sucres courants est le 2,5-diméthylfuranne, qui gêne dans le dosage de l'iodure d'alkyle par la méthode de Vieböck; les auteurs ont montré que ce produit était la cause des valeurs apparentes d'alkoxy. Les suggestions suivantes ont été réfutées: de l'iodure d'hexyle se dégage à partir des sucres, l'iodure de vinyle est un produit obtenu à partir des alcools polyhydriques.

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### 317. The Molecular Structure of Some Products from the Ehrlich-Sachs Reaction.

By D. M. W. ANDERSON and J. L. DUNCAN.

Several families of compounds, obtained as products of Ehrlich-Sachs-type reactions (reactive methylene compounds and aromatic nitroso-compounds), have been studied in solution by infrared spectroscopy. Deductions regarding the molecular structure of these compounds have been made. Several absorptions which occur at abnormal infrared frequencies are discussed.

THE Ehrlich-Sachs reaction, *i.e.*, the base-catalysed condensation of a reactive methylene compound with an aromatic nitroso-compound, has been the subject of recent investigations,<sup>1,2</sup> and the characteristic absorptions in the infrared spectra (obtained for mulls) of typical series of Ehrlich-Sachs products have been reported.<sup>2</sup>



In some of the series, striking variations in the absorptions given by homologous compounds were observed. Thus *N*-( $\alpha$ -cyano- $\alpha$ -ethoxycarbonylmethylene)-*N,N'*-dimethyl-*p*-phenylenediamine (I) gave a carbonyl absorption at 1740  $\text{cm}^{-1}$ , whereas its methoxy-analogue absorbed at 1708  $\text{cm}^{-1}$ . Moreover, *N*-( $\alpha$ -cyano- $\alpha$ -methoxycarbonylmethylene)-*N'*-methyl-*p*-phenylenediamine (II) existed in three crystalline modifications, (*a*) maroon needles, m. p. 170° (from methanol),  $\nu_{\text{C=O}}$  1687  $\text{cm}^{-1}$ , (*b*) yellow-orange needles, m. p. 170° (from benzene),  $\nu_{\text{C=O}}$  1713  $\text{cm}^{-1}$ , and (*c*) dark red prisms with blue fract, m. p. 168° (from the benzene mother-liquor),  $\nu_{\text{C=O}}$  1733 and 1706  $\text{cm}^{-1}$ .

These and certain other features of the spectra obtained indicated that the compounds merited further examination. Analytical specimens of the various series of compounds were kindly placed at our disposal for this purpose by Professor F. Bell, who has described their method of preparation.<sup>1,2</sup>

*Experimental.*—A Hilger H800 spectrophotometer fitted with a sodium chloride prism was used. Calibration was effected with reference to pyrrole vapour (3530  $\text{cm}^{-1}$ ), polystyrene film (3029 and 2923  $\text{cm}^{-1}$ ), dichloroacetonitrile (2261  $\text{cm}^{-1}$ ), and acetone vapours (1742  $\text{cm}^{-1}$ ), and is believed to be accurate to  $\pm 10$   $\text{cm}^{-1}$  in the  $\text{N-H}_{\text{st}}$  absorption region,  $\pm 5$   $\text{cm}^{-1}$  in the  $\text{C:N}$  absorption region, and  $\pm 2$   $\text{cm}^{-1}$  for carbonyl absorptions. Solutions in carbon tetrachloride or in chloroform (0.005—0.02M) were examined in a matched pair of variable-path-length cells fitted with sodium chloride windows. Solvent absorptions were removed by compensation in the reference beam. Absorptions are quoted as  $\text{cm}^{-1}$ .

*Ehrlich-Sachs Dinitriles.*—Table I gives the cyano-absorption frequencies of *N*-dicyanomethylene-*N,N'*-dialkyl-*p*-phenylenediamines as solids and as 0.01M-solutions in chloroform. (Certain of the mull absorptions previously given<sup>2</sup> are corrected.)

TABLE I. *Cyano-absorptions of 4,2,1-RR'N·C<sub>6</sub>H<sub>3</sub>R''·N:C(CN)<sub>2</sub>.*

R	R'	R''	C:N (mull)	C:N (solution)
Me	Me	H	2216, 2197	2227, 2212sh
Me	Et	H	2212, 2202sh	2224, 2211sh
Et	Et	H	2213 (1 peak only)	2223, 2209sh
Me	Me	Me	2214, 2198	2221, 2210sh
Et	Et	Me	2214, 2198	2223, 2210sh

Space-filling models of these molecules show that the two cyano-groups exist in markedly different environments, as illustrated by (III), the least steric hindrance being given when the  $\text{-N:C(CN)}_2$  group is perpendicular to the plane of the benzene ring. The cyano-group

lying in close proximity to the benzene ring will be subject to interaction with the  $\pi$ -electron cloud. Despite non-planarity of the molecule, the cyano-group remote from the benzene ring can be conjugated to the latter by interaction of the ring  $\pi$ -cloud, N atom lone-pair, N:C  $\pi$ -cloud and C:N  $\pi$ -cloud. It is therefore proposed that the cyano-group remote from the benzene ring absorbs at  $2210 \pm 2 \text{ cm.}^{-1}$ , the cyano-group in close proximity to the ring absorbing at  $2224 \pm 3 \text{ cm.}^{-1}$ . The validity of these deductions is supported by the behaviour in solution of the Ehrlich-Sachs esters discussed below.

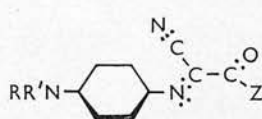
Table 1 shows that the presence of a methyl group in the 2-position of the ring ( $R''$  in Table 1) does not alter the absorption frequency of either cyano-group, although greater steric hindrance to free rotation is created. A study of models, however, shows that the configuration which departs least from planarity and so has the greatest stability is given when the cyano-group and the hydrogen atom in the 6-position are in close proximity. The preferred molecular configuration will, therefore, not be changed by introduction of a methyl group into the 2-position. This effect also applies to the other series of compounds discussed in this paper.

*Ehrlich-Sachs Esters.*—Table 2 lists the cyano and carbonyl absorption frequencies of *N*-( $\alpha$ -cyano- $\alpha$ -alkoxycarbonylmethylene)-*N'**N'*-dialkyl-*p*-phenylenediamines ( $R' = \text{Me, Et}$ ) and of *N*-( $\alpha$ -cyano- $\alpha$ -alkoxycarbonylmethylene)-*N'*-alkyl-*p*-phenylenediamines ( $R' = \text{H}$ ) as mulls and as 0.005M-solutions in carbon tetrachloride.

TABLE 2. *Cyano- and carbonyl absorption of 4,2,1-RR'N·C<sub>6</sub>H<sub>3</sub>R''·N:C(CN)·CO<sub>2</sub>R'''.*

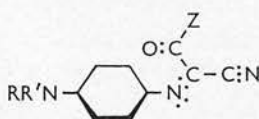
R	R'	R''	R'''	C:N		C:O	
				Mull	Soln.	Mull	Soln.
Me	Me	H	Me	2220	2212	1708	1757, 1731
Me	Me	H	Et	2200	2213	1740	1754, 1724
Et	Et	Me	Et	2200	2207	1694	1750, 1722
Et	H	H	Et	2220 orange 2202 maroon	{ 2211	{ 1750 1726	{ 1756, 1726
Me	H	H	Me	2210 orange 2198 maroon	{ 2216	{ 1713 1687	{ 1760, 1733
Et	H	H	Me	2210	2214	1731	1760, 1733
Me	H	H	Et	2215	2216	1741	1756, 1727

The marked variations in both the carbonyl and the cyano-absorption frequencies given by mulls disappear when the compounds are studied in solution, which give two carbonyl bands. The low and constant single absorption ( $2211 \pm 5 \text{ cm.}^{-1}$ ) of the cyano-group indicates, in terms of the deduction already made concerning cyano-groups, that of the two possible geometrical isomers (IV) and (V) the latter is preferentially formed under the reaction conditions used.<sup>1</sup>



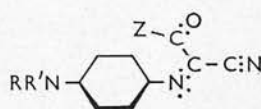
(IV)  $Z = \text{OR}'''$

(IX)  $Z = \text{NH}_2$



(V)  $Z = \text{OR}'''$

(VII)  $Z = \text{NH}_2$



(VI)  $Z = \text{OR}'''$

(VIII)  $Z = \text{NH}_2$

The occurrence of a single C:O frequency in the solids and of two in the solutions is clear evidence that the molecules can exist as rotational isomers, as represented by (V) and (VI).

Models show that whilst rotation can take place about the  $\text{C-CO}_2\text{R}'''$  bond, no free rotation is possible about the  $\text{N-ring}$  bond. In (V), the carbonyl group is in close proximity to the  $\pi$ -cloud of the benzene ring, and the resulting interaction will raise the carbonyl

frequency. (An  $\alpha$ -activated  $\alpha\beta$ -unsaturated ester would be expected<sup>3</sup> to give absorption in the range 1735–1750  $\text{cm}^{-1}$ .) In (VI), the OR''' group is in close proximity to the  $\pi$ -cloud of the benzene ring. This will result in an increased contribution from the  $\text{R}'''\text{O}^+:\text{C}-\text{O}^-$  polar canonical form to the carbonyl absorption. This resonance form may be further stabilised by interaction of the opposed formal charges on the carbonyl-oxygen atom and the closely adjacent carbon atom of the cyano-group. Thus the carbonyl frequency of isomer (VI) should be considerably lower than that of (V); the assignments of  $1755 \pm 5$  and  $1725 \pm 5$   $\text{cm}^{-1}$  can be made to (V) and (VI) respectively.

Temperature-dependence measurements were made to investigate the relative stabilities of the two isomers (V) and (VI) for each member of the series. In every case the intensity of absorption of the 1725  $\text{cm}^{-1}$  band increased with temperature. Isomer (VI) is therefore the less stable form.<sup>4</sup> The fact that the more stable form is that in which the opposition of like charges is greater has been previously discussed,<sup>4</sup> but is apparently not yet fully understood.

The variations in the carbonyl absorptions of the solids can be attributed to the fixation of one or other isomer, consistent with the production of the lattice of lowest energy. Two of the compounds studied (see Table 2) were isolated in two crystal forms. Use of a Kofler hot-stage microscope showed that in each case one of the forms was unstable, having a transition temperature below the true melting point at which it irreversibly changed, accompanied by a change in colour and crystal structure, to the more stable crystallographic form. Thus the maroon form of *N*-( $\alpha$ -cyanoethoxycarbonylmethylene)-*N'*-ethyl-*p*-phenylenediamine changed at 86° to the orange form (m. p. 107°); for *N*-( $\alpha$ -cyanomethoxycarbonylmethylene)-*N'*-methyl-*p*-phenylenediamine the orange form changed at 158° to the maroon form (m. p. 170°). Infrared studies of the temperature-dependence of these two compounds showed that, at the transition temperature, two carbonyl absorptions were given, one of which slowly decreased in intensity as the temperature was gradually raised, finally leaving the other as a single band. When the compound eventually melted, the two bands reappeared.

These examples of rotational isomerism support the initial assignments to the cyano-frequencies in Ehrlich-Sachs dinitriles: if the assignments be reversed, leading to (IV) in place of (V), models show that, although rotational isomerism of the ester group is still possible, an explanation of the large differences in the two carbonyl absorptions can no longer be found.

*Ehrlich-Sachs Amides.*—0.01M-Solutions in chloroform of several *N*-carbamoylcyanomethylene-*N'*-dialkyl-*p*-phenylenediamines all showed a cyano-band at  $2211 \pm 3$   $\text{cm}^{-1}$ . The assignment for cyano-groups therefore favours the structure (VII), or its possible rotational isomer (VIII), rather than (IX). In the carbonyl absorption region, bands were present at  $1694 \pm 2$  (s),  $1618 \pm 1$  (s), and at 1555 (w) and 1495 (s). When each compound was studied in a range of solvents of varying polarity,<sup>5</sup> the 1694  $\text{cm}^{-1}$  band varied between 1710  $\text{cm}^{-1}$  ( $\text{CCl}_4$ ) and 1691  $\text{cm}^{-1}$  ( $\text{CHBr}_3$ ), whilst the other three bands remained constant. A  $\text{d}\nu/\nu$  plot (based on carbon tetrachloride) for the 1691–1710  $\text{cm}^{-1}$  band against acetophenone<sup>5</sup> gave a straight line. Hence only one carbonyl band is given in solution, the 1618  $\text{cm}^{-1}$  band being attributed to the N:C bond. Rotational isomerism, although feasible on steric grounds, is therefore not exhibited by these amides.

It is well known that the contribution of the polar canonical form  $\text{H}_2\text{N}^+:\text{C}-\text{O}^-$  in amides is considerable, and is responsible<sup>3</sup> for occurrence of the carbonyl absorption normally near 1690  $\text{cm}^{-1}$  for dilute solutions. An  $\alpha$ -activated  $\alpha\beta$ -unsaturated amide would also be expected to give a carbonyl band near 1690  $\text{cm}^{-1}$ . The observed 1691–1710  $\text{cm}^{-1}$  band, therefore, indicates that an activation effect on the carbonyl group is tending to reduce the  $\text{H}_2\text{N}^+:\text{C}-\text{O}^-$  contribution: this effect would be given in structure (VII), on the basis of the reasoning in the discussion of Ehrlich-Sachs esters. Structure (VIII) would involve increased contribution by the form  $\text{H}_2\text{N}^+:\text{C}-\text{O}^-$ , leading to an absorption frequency

much lower than that normally exhibited by amides. It is concluded that in structure (IX) the charge-distribution effects become so great that this isomer is unstable.

The compound *N*-carbamoylcyanomethylene-*N'**N'*-di-*n*-propyl-*p*-phenylenediamine<sup>1</sup> was, however, found to give two carbonyl bands at 1714w and 1657s cm.<sup>-1</sup> in the solid state. For the liquid state and for chloroform solution only one band at 1694 cm.<sup>-1</sup> was given. Repeated purification failed to yield material in which the 1714 cm.<sup>-1</sup> band was absent from the solid-state spectrum. Identical spectra were given by crystals grown from different solvents and from cast films: the possibility of the presence of dimorphic crystal forms is therefore small. The cause of this effect was not determined. A similar crystal effect was given by *N*-( $\alpha$ -cyano- $\alpha$ -methoxycarbonylmethylene)-*N'*-methyl-*p*-phenylenediamine (II) (see Table 2); on one occasion a third isomer, strongly crystalline and giving absorptions at 1733m and 1706m cm.<sup>-1</sup>, was obtained. On melting, the compound crystallised as the stable yellow-orange isomer, giving absorption at 1713 cm.<sup>-1</sup>. Numerous recrystallisation attempts failed to yield any further quantity of the third isomer, which would appear to have been formed by the simultaneous crystallisation of both rotational isomers.

*Condensations involving 2 Mols. of Cyanoacetic Esters and Condensations between Dinitriles and Esters.*—These respectively produce *N*-(2-cyano-1,2-dialkoxycarbonylvinyl)-*N'**N'*-dialkyl-*p*-phenylenediamines and *N*-(1,2-dicyano-2-alkoxycarbonylvinyl)-*N'**N'*-dialkyl-*p*-phenylenediamines<sup>2</sup> (see Table 3a and b respectively). It was suggested<sup>2</sup> on infrared evidence that these contained an N-H group; this has now been confirmed by alkaline hydrolysis to the corresponding *NN*-dialkyl-*p*-phenylenediamines, which were characterised as their acetyl and benzoyl derivatives.<sup>6</sup>

When both series of compounds were studied as mulls, their characteristic NH, CN, and CO frequencies were little influenced by the nature of the alkyl groups. For each series, the variation between compounds is shown in Table 3.

Each compound in the two series was then studied in solution (0.01M) in each of the following solvents: carbon tetrachloride, methylene chloride, chloroform, diethyl ether, nitromethane, and bromoform. The NH and CO frequencies of each varied little with change of solvent; Table 3 shows the maximum frequency shift given by any of the compounds of each series.

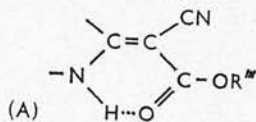
TABLE 3. *Solid and solution spectra: (a) 4,2,1-RR'N·C<sub>6</sub>H<sub>3</sub>R''·NH·C(CO<sub>2</sub>R'''):C(CN)·CO<sub>2</sub>R'''*,  
(b) 4,2,1-RR'N·C<sub>6</sub>H<sub>3</sub>R''·NH·C(CN):C(CN)·CO<sub>2</sub>R'''

N-H			C≡N		C=O					
Mull *	Soln.*	Solvent †	Mull *	Soln.*	Solvent †			Solvent †		
		vartn. †			Mull *	Soln.*	vartn. †	Mull *	Soln.*	vartn. †
(a) 3275	3215	±5	2228	2222	1755	1755	±7	1675	1675	±2
±20	±10		±8	±5	±5	±5		±5	±5	
(b) 3235	3220	±10	2222	2220	—	—	—	1688	1678	±3
±35	±20		±12	±5				±6	±6	
										(1 peak only)

\*  $\pm x$  = limits of variation between compounds in the series.

† Max. frequency shift of any compound when examined in solvents of differing polarities.

In these compounds, the low frequencies of the N-H absorption and of a carbonyl absorption suggest the existence of strong intramolecular hydrogen bonding. Models show that group (A) (inset) forms a compact six-membered ring system; the frequency 1675 cm.<sup>-1</sup> is therefore assigned to this ester group. The variation of this band in different solvents is small,  $\pm 3$  cm.<sup>-1</sup> (Table 3); this is consistent with strong intramolecular hydrogen bonding, which prevents normal interaction of proton-donating solvents with the C:O link.<sup>7</sup> The second ester group (1755 cm.<sup>-1</sup>) in series (a) (Table 3) suffers severe steric hindrance and is almost 90° out of plane with respect to



the C:C bond. The absorption frequency observed is therefore more typical of a saturated ester than of an  $\alpha\beta$ -unsaturated ester (cf. ref. 8).

*The Colour of N-(2-Alkoxy-carbonyl-1,2-dicyanovinyl)-N'N'-dialkyl-p-phenylenediamine.*— These compounds lack extended conjugation but are dark red. Solutions in chloroform showed a broad band with  $\lambda_{\text{max}}$  453  $m\mu$ . A study of very dilute solutions ( $5 \times 10^{-4}$  to  $5 \times 10^{-5}M$ ) in chloroform in 1–10 mm. quartz cells showed that the intensity of the 453  $m\mu$  band decreased rapidly with decreasing concentration, whilst a new band ( $\lambda_{\text{max}}$  346  $m\mu$ ) increased in intensity. The spectra exhibited an isosbestic point at 394  $m\mu$ ; two species were therefore present in solution.

To investigate this effect, a series of tricyanovinylanilines,  $R \cdot C_6H_4 \cdot NH \cdot C(CN) : C(CN)_2$ , was prepared,<sup>6</sup> where R = H, Me, Et, Pr<sup>i</sup>, Bu<sup>t</sup>, OMe, and NMe<sub>2</sub>. The series therefore had increasing electron-donation from the R groups in the *para*-position. The series ranged in colour from pale yellow for R = H to orange for R = OMe, but the R = NMe<sub>2</sub> compound was deep maroon. The yellow series had  $\lambda_{\text{max}}$  ranging from 348  $m\mu$  for R = H to 362  $m\mu$  for R = OMe ( $5 \times 10^{-4}M$ -solutions in chloroform); this absorption is clearly due to the simple molecule. For *p*-NN-dimethyltricyanovinylaniline, however, the visible band (445  $m\mu$ ) decreased with decreasing concentration in very dilute solutions ( $5 \times 10^{-4}$  to  $5 \times 10^{-6}M$  in chloroform) whilst a band at 370  $m\mu$  simultaneously increased. An isosbestic point occurred at 403  $m\mu$ .

The anomalous deep colour of *p*-NN-dimethyltricyanovinylaniline and of the series of *N*-(2-alkoxy-carbonyl-1,2-dicyanovinyl)-*N'N'*-dialkyl-*p*-phenylenediamines may therefore be attributed to some form of self- $\pi$ -complexing arising from the particular molecular structure. The complex is destroyed at very high dilutions, with liberation of the simple molecules which absorb in the expected ultraviolet region.

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<sup>1</sup> Bell, *J.*, 1957, 516.

<sup>2</sup> Anderson and Bell, *J.*, 1959, 3708.

<sup>3</sup> Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., London, 1958, 2nd edn., pp. 179, 205.

<sup>4</sup> Bellamy, Thomas, and Williams, *J.*, 1956, 3704.

<sup>5</sup> Bellamy and Rogasch, *Spectrochim. Acta*, 1960, **16**, 30.

<sup>6</sup> McKusick, Heckert, Cairns, Coffman, and Mower, *J. Amer. Chem. Soc.*, 1958, **80**, 2806.

<sup>7</sup> Bellamy and Hallam, *Trans. Faraday Soc.*, 1959, **55**, 220; Bellamy and Rogasch, *J.*, 1960, 2218.

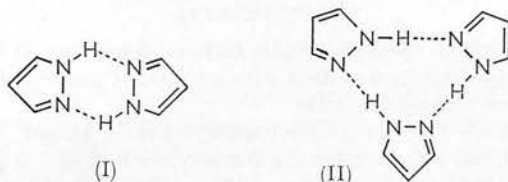
<sup>8</sup> Felton and Orr, *J.*, 1955, 2170.

## 26. *The Hydrogen Bonding of Pyrazole in Carbon Tetrachloride Solution.*

By D. M. W. ANDERSON, J. L. DUNCAN, and F. J. C. ROSSOTTI.

Analysis of the concentration-dependence of the infrared spectrum of pyrazole in carbon tetrachloride at  $18^\circ \pm 1^\circ$  has shown that the fundamental N-H stretching band at  $3485 \pm 10 \text{ cm.}^{-1}$  is due to monomeric pyrazole only. Hydrogen-bonding equilibria in the concentration range  $10^{-4}$ —1M have been interpreted quantitatively in terms of co-existing monomer, cyclic dimer, and cyclic trimer, with overall formation constants of  $\beta_{20} = 47.5 \pm 1.0 \text{ l. mole}^{-1}$  and  $\beta_{30} = 7540 \pm 240 \text{ l.}^2 \text{ mole}^{-2}$ .

HÜCKEL and his co-workers<sup>1</sup> have suggested, on the basis of cryoscopic, viscometric, and dielectric measurements, that pyrazole consists predominantly of a cyclic, hydrogen-bonded dimer (I) at moderate concentrations in non-associated solvents. It was also suggested that more than two monomers might form chains at higher concentrations.



Hunter<sup>2</sup> has recently criticised the non-linear hydrogen bond in (I) and suggested that the strainless cyclic trimer (II) would be more stable. A cryoscopic study of 3,5-dimethylpyrazole in benzene by White and Kilpatrick<sup>3</sup> has given convincing evidence for the existence of a stable trimer, and dubious evidence for an unstable dimer. These authors consider that the trimer is almost certainly cyclic, and the dimer most probably linear. An X-ray analysis by Ehrlich<sup>4</sup> has now shown that pyrazole exists in the solid state as long, parallel, hydrogen-bonded chains, which describe figure-of-eight spirals. The present study was undertaken to investigate the nature of the pyrazole oligomers which exist in carbon tetrachloride solution.

A preliminary study of dilute solutions of pyrazole in carbon tetrachloride showed a fundamental N-H stretching mode at  $3485 \pm 10 \text{ cm.}^{-1}$  with a half-band width of  $20 \text{ cm.}^{-1}$ . The intensity of this band decreased with increasing total concentration,  $B$ ; concurrently, a broad, bonded N-H band of increasing intensity appeared in the region  $3400$ — $2000 \text{ cm.}^{-1}$

<sup>1</sup> Hückel, Datow, and Simmersbach, *Z. phys. Chem.*, 1940, **186**, A, 129; Hückel and Jahnentz, *Ber.*, 1942, **75**, 1438.

<sup>2</sup> Hunter, in "Progress in Stereochemistry," ed. Klyne, Butterworths, London, 1954, p. 223.

<sup>3</sup> White and Kilpatrick, *J. Phys. Chem.*, 1955, **59**, 1044.

<sup>4</sup> Ehrlich, *Acta Cryst.*, 1960, **13**, 946.

*Bonded N-H absorption bands of pyrazole (all peaks strong).*

Solid (cast film) .....	3135	3050	2960	2900	2860	2810(sh)
CCl <sub>4</sub> solution .....	3175	3070	2995	2930	2905	2825(sh)

(see Fig. 1); this showed six major peaks [excluding that due to C-H at 3120 cm.<sup>-1</sup> (w)], which were remarkably similar to the infrared N-H absorption bands of a solid, cast film of pyrazole. A quantitative study was therefore made of the concentration-dependence of the intensity of the 3485 cm.<sup>-1</sup> band.

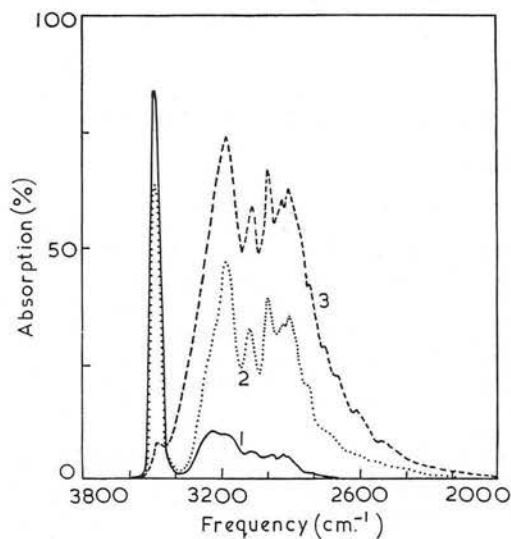


FIG. 1. *Infrared absorption spectra in the region 3800—2000 cm.<sup>-1</sup> for carbon tetrachloride solutions of pyrazole at various total concentrations, B, at 18°.*

1,  $B = 0.001M$ . 2,  $B = 0.010M$ .  
3,  $B = 1.00M$ .

## EXPERIMENTAL

*Materials.*—Pyrazole was recrystallised twice from cyclohexane; it had m. p. 70° (lit., 70°). Reagent-grade carbon tetrachloride was used without further purification; no O-H absorption spectrum was detectable on using 4 cm. cells.

*Infrared Measurements.*—The spectrophotometer was a Hilger H800 double-beam instrument. A rock-salt prism was used for preliminary studies, and a quartz prism for precise measurements on dilute solutions ( $B < 10^{-2}M$ ). The quartz prism gave a theoretical slit-width of 8 cm.<sup>-1</sup> at 3485 cm.<sup>-1</sup> with a spectrometer slit-width of 0.30 mm. The frequency scale was calibrated with reference to the N-H stretching frequency of pyrrole vapour (3530 cm.<sup>-1</sup>). The spectrophotometer was not thermostatically controlled, and wave-number estimates are

TABLE I. *Infrared absorbancies at 3485 cm.<sup>-1</sup> of associated pyrazole in carbon tetrachloride at 18° ± 1°.*

$10^4 B$ ...	0.9947	1.989	2.984	3.979	4.974	5.968	6.963	7.958	8.952	9.947	
$\log I_0/I...$	0.0894*	0.174*	0.260*	0.347*	0.417*	0.494*	0.574*	0.646*	0.721*	0.0985	
$10^4 B$ .....	11.94	13.93	15.92	17.91	19.89	21.88	23.87	25.86	27.85	29.84	31.83
$\log I_0/I...$	0.118	0.134	0.150	0.167	0.179	0.193	0.210	0.222	0.235	0.244	0.257
$10^4 B$ .....	33.82	35.81	37.80	39.79	41.78	43.77	45.76	47.75	49.74	51.72	53.71
$\log I_0/I...$	0.271	0.287	0.295	0.305	0.314	0.329	0.336	0.346	0.351	0.363	0.373
$10^4 B$ .....	55.70	57.69	59.68	61.67	63.66	65.65	67.64	69.63	71.62	73.61	75.60
$\log I_0/I...$	0.385	0.394	0.399	0.408	0.419	0.426	0.434	0.438	0.447	0.457	0.467

\* 4.00 cm. cells: all other results refer to 0.500 cm. cells.

considered to be accurate to ±10 cm.<sup>-1</sup> within the region 3500—3000 cm.<sup>-1</sup>. Run-to-run reproducibility was ±5 cm.<sup>-1</sup>. Instrumental conditions were: gain, 4; damping, 2; speed of scan, 68 cm.<sup>-1</sup>/min. Variable path-length cells, set at 5.000 ± 0.005 mm. and fitted with



The standard deviations of the slope and intercept were found to be  $\pm 716$  and  $\pm 2$  by an unweighted least-squares treatment.

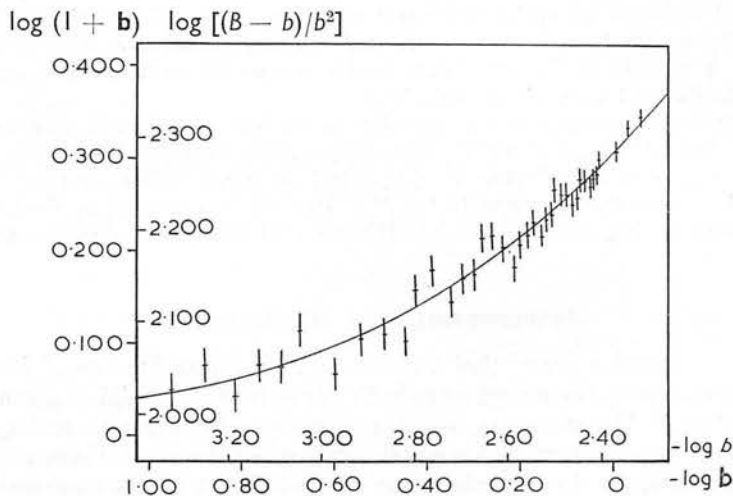
The significance of the experimental eqn. (5) follows from a consideration of the four possible combinations of linear and cyclic oligomers,  $B_2$  and  $B_3$ . The experimental variables  $(B - e)/e^2$  and  $e$  are expressed in terms of  $b$  by using eqns. (3) and (4) for the four possibilities in Table 2.

TABLE 2. *The possible variables of eqn. (5) for the pyrazole system in carbon tetrachloride.*

$B_2$	$B_3$	$(B - e)/e^2$	$e$
Cyclic	Cyclic	$2\beta_{20} + 3\beta_{30}b$	$b$
Linear	Linear	$(\beta_{20} + 2\beta_{30}b)/(1 + \beta_{20}b + \beta_{30}b^2)^2$	$b + \beta_{20}b^2 + \beta_{30}b^3$
Cyclic	Linear	$(2\beta_{20} + 2\beta_{30}b)/(1 + \beta_{30}b^2)^2$	$b + \beta_{30}b^3$
Linear	Cyclic	$(\beta_{20} + 3\beta_{30}b)/(1 + \beta_{20}b)^2$	$b + \beta_{20}b^2$

It is apparent that  $(B - e)/e^2$  will be linear in  $e$  if the free N-H band is in fact due to monomeric pyrazole only, and the dimer and trimer are both cyclic. However, it is

FIG. 2. *The experimental data  $\log \{(B - b)/b^2\}$  plotted as a function of  $\log b$  superimposed in the position of best fit on the normalised curve  $\log (1 + b)$  as a function of  $\log b$ .*



extremely unlikely that a linear representation of the data according to eqn. (5) would have been found, if either or both the associated species were linear. We therefore derive from eqn. (5) values of

$$\beta_{20} = 47.4 \pm 1.0 \text{ l. mole}^{-1} \text{ and } \beta_{30} = 7540 \pm 240 \text{ l.}^2 \text{ mole}^{-2}$$

The values of the association constants were checked by the curve-fitting method suggested by Rossotti and Rossotti.<sup>7</sup> The expression

$$\log \left( \frac{B - b}{b^2} \right) - \log 2\beta_{20} = \log \left( 1 + \frac{3\beta_{30}}{2\beta_{20}} b \right)$$

is a rearrangement of eqn. (3). The experimental data,  $\log \{(B - b)/b^2\}$  plotted as a function of  $\log b$ , will therefore be of the same shape as the normalised curve  $\log (1 + b)$

<sup>7</sup> Rossotti and Rossotti, "The Determination of Stability Constants," McGraw-Hill, New York, in the press, Chap. 16.

plotted as a function of  $\log b$ . The experimental and normalised curves are superimposed, and, in the position of best fit (see Fig. 2), the equations

$$\log(1 + b) = \log[(B - b)/b^2] - \log 2\beta_{20}$$

and

$$\log b = \log b + \log(3\beta_{30}/2\beta_{20})$$

may be solved for  $\beta_{20}$  and  $\beta_{30}/\beta_{20}$ . The permissible relative displacements of the experimental and the normalised curves, parallel to the co-ordinate axes, give estimates of the errors in the two parameters. Hence, we obtain values of

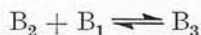
$$\beta_{20} = 47.5 \pm 1.0 \text{ l. mole}^{-1} \text{ and } \beta_{30} = 7540 \pm 300 \text{ l.}^2 \text{ mole}^{-2}$$

in excellent agreement with the values obtained from the linear equation. This treatment therefore confirms that monomer, cyclic dimer, and cyclic trimer are the only species co-existing in the concentration range  $10^{-4} \leq B \leq 10^{-2}$  M. There is no evidence for detectable concentrations of larger oligomers.

#### DISCUSSION

The percentage distribution of pyrazole between the monomer, cyclic dimer, and cyclic trimer has been calculated as a function of the total concentration of pyrazole by using eqn. (3), and is shown in Fig. 3. The precise infrared measurements from which the equilibria have been deduced only extend up to  $B = 10^{-2}$  M, where the pyrazole is approximately 25% dimeric and 37% trimeric. However, the percentages of monomer, which may be derived from the less precise data in the range  $10^{-2} \leq B \leq 1$  M, are in good agreement ( $\pm 4\%$ ) with the values calculated by using eqn. (3). Our values of  $\beta_{20}$  and  $\beta_{30}$  therefore represent the pyrazole system at 18° in carbon tetrachloride for total concentrations  $B \leq 1$  M.

It is evident from the value of  $\beta_{20}$  and  $\beta_{30}$  that the trimer is much more stable than the dimer. The equilibrium constant for the reaction



is given by  $\beta_{30}/\beta_{20} = 159 \pm 61 \text{ l. mole}^{-1}$ , as compared to the dimerisation constant of  $47.5 \text{ l. mole}^{-1}$ .

As the pyrazole molecule is planar, the cyclic dimer and trimer will also be planar. Consideration of Ehrlich's structure<sup>4</sup> for the long chains of pyrazole molecules in the solid state suggests that the N-H-N bond in the cyclic trimer may not be quite linear.

An examination of the bonded N-H region, from the viewpoint of the calculated distribution of pyrazole oligomers, suggests that the bands at 3175, 3070, 2995, 2930, 2905, and 2825  $\text{cm.}^{-1}$  may be assigned to the trimer. The relative intensities of these bands remain unchanged as  $B$  varies. The dimer appears to contribute a leading edge to the band at 3175  $\text{cm.}^{-1}$ . This absorption becomes a significant shoulder when  $B < 10^{-2}$  M, and the concentration of dimer exceeds that of trimer. However, the absorption of the trimer is much stronger than that of the dimer, and the shoulder is not detectable for  $B > 10^{-2}$  M (cf. Figs. 1 and 3). The absorption band of the dimer would be expected to be at a higher frequency than that of the trimer on the basis of Badger's correlation<sup>8</sup> of frequency shift with the energy of the hydrogen bond. Moreover, it has been shown<sup>9</sup> that non-linear intramolecular hydrogen bonds are associated with smaller frequency shifts than linear hydrogen bonds. The frequency shifts for both dimer and trimer clearly correspond to

<sup>8</sup> Badger, *J. Chem. Phys.*, 1940, **8**, 288.

<sup>9</sup> Nakamoto, Māgoshes, and Rundle, *J. Amer. Chem. Soc.*, 1955, **77**, 6480.

very short N-H-N bond lengths (cf. ref. 9). Indeed, the figure-of-eight spirals of pyrazole in the solid state<sup>4</sup> contain N-H bonds of length  $\sim 2.9$  Å. The shortness of these bonds, and also the tendency to self-association in solution, are presumably both due to a markedly unequal distribution of charge on the two nitrogen atoms of a molecule of pyrazole. The assignment of six bands in the bonded N-H region to a single species is of some interest in connection with current theories of the structure of X-H stretching modes.<sup>10,11</sup>

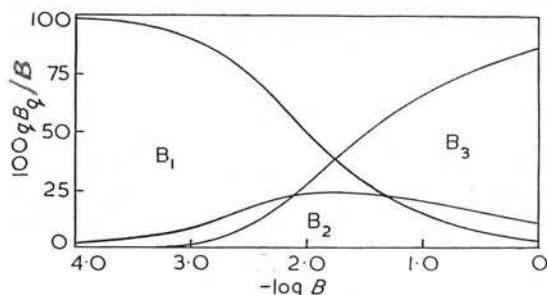


FIG. 3. The percentage distributions  $100qB_q/B$  of the pyrazole species in carbon tetrachloride at  $18^\circ$  plotted as a function of  $\log B$ .

The intensities of the observed N-H bands were markedly sensitive to temperature. With increase of temperature, the intensity of the  $3485\text{ cm}^{-1}$  band due to free pyrazole increased, and that of the broad, bonded N-H band decreased. This implies that the enthalpy changes on association are negative, always provided that the temperature variation of the apparent extinction coefficients is not a dominant factor.<sup>12</sup> As the temperature coefficient of the dielectric constant of carbon tetrachloride is approximately zero,<sup>13</sup> the negative enthalpies appear to be partly due to non-environmental exchange forces. It is therefore possible that the covalent contribution to the hydrogen bond is more important than is commonly supposed.

The infrared spectra of pyrazole in other non-associated solvents, *e.g.*, carbon disulphide and chloroform, are qualitatively similar to that in carbon tetrachloride. It is therefore likely that the same equilibria obtain.

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<sup>10</sup> Bratož and Hadži, *J. Chem. Phys.*, 1957, **27**, 991; Pimentel and McClellan, ref. 6, p. 102.

<sup>11</sup> Sheppard, in "Hydrogen Bonding," eds. Hadži and Thompson, Pergamon Press, London, 1959, p. 85.

<sup>12</sup> Becker, in ref. 11, p. 155; Pimentel and McClellan, ref. 6, p. 76.

<sup>13</sup> Landolt-Börnstein, "Tabellen," II, (6), "Elektrische Eigenschaften 1," Springer-Verlag, Berlin, 1959, p. 625.