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THE USE OF GAS CHROMATOGRAPHIC DETECTORS FOR MOLECULAR WEIGHT DETERMINATIONS

S. C. BEVAN, T. A. GOUGH* AND S. THORBURN
Chemistry Department, Brunel University, London, W.3 (Great Britain)
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SUMMARY

The molecular weights of the constituents of mixtures may be determined, after chromatographic separation, using a detector whose response is a function of molecular weight. Various methods are discussed and results presented for a mass detector/gas density balance system, by which molecular weights may be determined from a single analysis.

INTRODUCTION

An ideal procedure for the determination of the molecular weights of the constituents of a mixture would comprise the separation of the constituents by gas chromatography, and at the same time, the use of the detector response to determine the molecular weight of each component as it emerged. Present methods require pure and isolated materials: ebullioscopic and cryoscopic methods are straightforward, but give only moderate accuracy. Mass spectrometry gives very accurate results but demands expensive equipment. Using a gas chromatographic detector whose response depends solely on molecular weight, the accuracy of the method will depend on the accuracy to which peak areas can be measured. The response of the gas density balance[1], the jet stream detector[2], and the ultrasonic detector[3] is a function of molecular weight. The gas density balance has been used by several workers for molecular weight determinations[4-9], but no data have been published using the remaining detectors.

DISCUSSION

The response of the gas density balance is given by the equation:

$$A = kq \frac{M_x - M_c}{M_x} \quad (1)$$

where q = amount of component x, M_x = molecular weight of x, A = peak area, and M_c = molecular weight of carrier gas. The proportionality constant k, can be found by measuring the response to a known amount of a pure material of known

* Present address: Laboratory of the Government Chemist, Stamford Street, London, S.E.1.

molecular weight. By injecting under identical conditions a known amount of an unknown material, its molecular weight can be calculated, using eqn. 1. In practice this method is open to a number of serious objections. It is not possible merely to separate the constituents of a mixture in the gas chromatographic column, and to determine the molecular weight of each component as it emerges, since values for q for each component are not known. Both the standard material and the unknowns are required in the pure isolated state. In addition it is particularly difficult to inject a known amount of material into the apparatus, and to ensure that no fraction is lost before reaching the detector. It is difficult to maintain precisely the same experimental conditions over the period of time required for calibration and subsequent analysis of unknowns. A satisfactory practical procedure for the determination of molecular weights using a gas density balance was first carried out by LIBERTI *et al.*[5]. To an unknown mixture is added a compound of known molecular weight, M_s, and the mixture is analysed in the conventional manner. For a two-component mixture, two peaks of areas A_x and A_s for the unknown and standard, respectively, are obtained:

$$A_{x1} = kq_{x1}\frac{M_x - M_1}{M_x} \tag{2}$$

and

$$A_{s1} = kq_{s1}\frac{M_x - M_1}{M_s} \tag{3}$$

where M_1 = molecular weight of carrier gas 1.

The experiment is repeated using a carrier gas of different molecular weight, M_2, to give:

$$A_{x2} = kq_{x2}\frac{M_x - M_2}{M_x} \tag{4}$$

and

$$A_{s2} = kq_{s2}\frac{M_s - M_2}{M_s} \tag{5}$$

It is not essential to inject precisely the same quantity of the mixture in each series of runs since the ratio:

$$\frac{q_{x1}}{q_{s1}} = \frac{q_{x2}}{q_{s2}} \tag{6}$$

and by combining eqns. 2 to 5

$$\frac{A_{x1}(M_s - M_1)}{A_{s1}(M_x - M_1)} = \frac{A_{x2}(M_s - M_2)}{A_{s2}(M_x - M_2)} \tag{7}$$

The A values are obtained directly from the peak areas of the chromatograms, and all molecular weights are known except M_x, which can be calculated. Using nitrogen and hydrogen as the two carrier gases, molecular weights to about 4% of the true values were obtained for materials of molecular weight about 150 (ref. 5). Similar results were obtained by REVEL'SKII *et al.*[6] using nitrogen and argon. In an attempt to improve upon the accuracy of the results, PARSONS[7] used one carrier gas of molecular

weight lower than the unknown, and the other carrier gas of molecular weight higher than the unknown (*e.g.* nitrogen and dichlorodifluoromethane). Errors of the order of 1–2 % are quoted in the published data[7]. Molecular weight determinations based on the LIBERTI scheme, although giving acceptable results suffer from the disadvantage that column conditions must remain constant for the duration of the two sets of runs, although it is no longer necessary to know the amount of sample injected, or to work with pure isolated materials. The need to change the carrier gas is tiresome, but is not regarded as a very serious disadvantage.

An alternative method for determining molecular weights using the gas density balance was devised by PHILLIPS AND TIMMS[8]. Eqn. 1 is rearranged and rewritten:

$$PV = \frac{KA}{M_x - M_c} \tag{8}$$

where P and V are the pressure and volume of a vapour x, and K a constant. Pressure–volume (P–V) measurements are made on the vapour, which is then passed into a gas density balance. K is found using a material of known molecular weight. The method gives molecular weights, in general to within 1 % of the true values, for materials of boiling point up to about 200°. The P–V equipment requires considerable skill to operate and the determination of a single molecular weight is fairly time consuming. Pure isolated materials are required. Preparative chromatography or other methods of purification must therefore be employed before molecular weight determinations can be carried out.

A chromatographic method for the determination of molecular weights based on the measurement of the increase in flow rate which occurs as a component emerges from a column was proposed by SCOTT[10]. The gas volume, ΔV, occupied by m grams of solute vapour is given by the equation:

$$\Delta V = m \frac{K}{K+1} \times \frac{22.4 \times 10^3}{M} \times \frac{T}{273} \tag{9}$$

where K = partition coefficient and M = molecular weight of solute.

For a two-component mixture, containing one material of known molecular weight, M_s:

$$\frac{\Delta V_s}{\Delta V_x} = \frac{M_x m_s}{M_s m_x} \tag{10}$$

provided that $K \approx K + 1$.

If the detector responds solely to flow rate changes:

$$\frac{\Delta V_s}{\Delta V_x} = \frac{A_s}{A_x} \tag{11}$$

where A_s and A_x are peak areas representing the standard and the unknown, respectively. The molecular weight of the unknown is given by:

$$M_x = \frac{A_s m_x M_s}{A_x m_s} \tag{12}$$

It is essential to know the weights of the injected materials, which when using syringe injection implies that the densities of the standard and the unknown

must be known. The assumption that $K \gg 1$ will give rise to negligible errors provided that retention times are long and are similar for the standard and the unknown.

The flame thermocouple detector[11] is sensitive to both flow rate changes and changes in temperature caused by the presence of an eluted material. These two effects can be isolated by preventing the material from reaching the detector. The detector will then respond only to flow rate changes. SCOTT used the following system to accomplish this effect. The exit of a normal partition column was attached to a length of empty tubing which itself was attached to a column containing activated charcoal. A substance, on emerging from the partition column, produced a flow rate change which was detected as a positive peak by the flame thermocouple detector. On entering the adsorption column the material was totally adsorbed, resulting in a flow rate decrease, which was detected as a negative peak. By using the adsorption peak area rather than the partition peak area, the assumption that $K \gg 1$ is removed. Using the results quoted by SCOTT[10], the molecular weights of a number of materials determined by this method have been calculated, and are quoted in Table I.

TABLE I

MOLECULAR WEIGHT DETERMINATIONS (FLAME THERMOCOUPLE DETECTOR)

Compound	*Detector response (area/unit weight)*	*Molecular weight*		*Bias*
		Calculated	*True*	
n-Hexane (standard)	5.8	86.2	86.2	Standard
Carbon tetrachloride	3.2	156.2	153.8	+ 2.4
Chloroform	4.1	122.0	119.5	+ 2.5
Dichloroethylene	5.3	94.4	97.0	− 2.6
n-Butyl chloride	5.3	94.4	92.7	+ 1.7
Ethyl acetate	5.6	89.3	88.1	+ 1.2
Ether	6.8	73.5	74.2	− 0.7
Acetone	8.6	58.2	58.1	+ 0.1

Errors of the order of 2 % are encountered. On the assumption that the detector is responding only to flow rate changes, the major errors arise from the difficulty of injecting known weights of each material, and of measuring the resulting peak areas.

The requirement that the amount of injected material must be known (and hence densities known) is common to all of the detectors which can be used for molecular weight determinations, and constitutes the major limitation and error source in the determination of molecular weights by gas chromatography.

It has been established that the mass detector will give reliable quantitative analyses over a wide range of operating conditions, and that response is proportional to mass. If the mass detector is operated in conjunction with a detector responding to molecular weight changes, then the amount of material present is obtained directly from the mass detector response. A knowledge of the amount of material injected, its density, and the percentage composition of the mixture is not required, and losses of material within the column do not affect the results. It was demonstrated by BEVAN AND THORBURN[4] that by using a gas density balance and the mass detector in series, the molecular weights of the constituents of an unknown mixture could be found in a single run. Two chromatograms are obtained: the mass detector will give values of

r (eqn.1) for each material, and the gas density balance the corresponding values of A. The value of k is found by adding to the mixture a compound of known molecular weight. It is not necessary to add a precisely measured amount of standard. The only requirement is the same for any conventional quantitative analysis, namely that resolution of the components should be complete. It would appear that the use of the mass detector in conjunction with the gas density balance offers an ideal method for the determination of molecular weights. There are, however, two factors which limit the method:

(i) the calculation of a molecular weight depends on the accuracy with which a peak area and a step height can be measured, as with any other method involving gas chromatographic detectors.

(ii) the change in response of the gas density balance for species of different molecular weight is a maximum when values of M_c and M_x (eqn. 1) are of the same order: but the absolute response of the detector is a minimum when M_c and M_x are similar, and zero when they are equal. As the values of M_c and M_x diverge it becomes more and more difficult to distinguish between the responses of compounds of similar molecular weight; in the limiting case $(M_x—M_c)/M_x = 1$, and the molecular weight term disappears. The effect is shown graphically in Fig. 1 for a number of carrier gases covering the molecular weight range 4 to 121. It will not be possible to determine the molecular weight of a material with certainty if its molecular weight is at a point on or approaching the plateau of the curve. Consider the curve for nitrogen. It should be possible to determine the molecular weight of any material up to about 120, including values below that of nitrogen, but with decreasing certainty as the molecular weight increases. Over about 120, even a small discrepancy in the measurement of A will result in an error in the value of $(M_x—M_c)/M_x$, and the error in M_x itself will be grossly magnified.

For a detector to be of value for molecular weight determinations it is essential that the response depends only on molecular weight changes. It has previously been shown that the response of the Gow-Mac gas density detector is a function of molecular weight within certain limits[12]. It is generally accepted and has recently been demon-

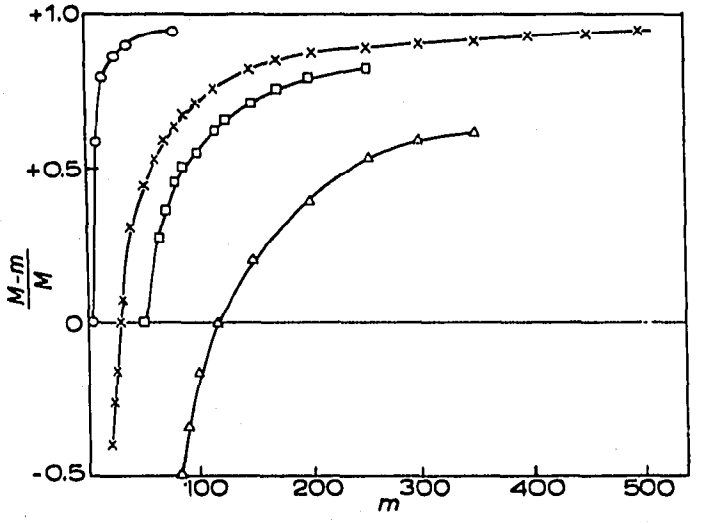

Fig. 1. The effect of carrier gas on molecular weight determinations. m = molecular weight of component; M = molecular weight of carrier. ○, helium; ×, nitrogen; □, carbon dioxide; △, dichlorodifluoromethane.

strated[13] that the Martin gas density balance gives a response predictable on a molecular weight basis, over a wide concentration range for all materials, and this detector was therefore used in the present work.

The fall in precision with increasing molecular weight limits the value of the gas density balance–mass detector combination. Combination of the mass detector with the flame thermocouple detector operated as an anemometer overcomes this limitation, since although the response of the flame thermocouple decreases as molecular weight increases, it does so linearly and hence a marked fall in precision does not occur. Using a combination of partition and adsorption to create flow rate changes, it would appear to be necessary to operate the two detectors in parallel. However, the incorporation of a stream splitting device may interfere with the flow rate pattern as a material is eluted. Preferably, the two detectors should be operated without the need for a stream splitter. This may be accomplished by replacing the adsorption column with a second short partition column. Elution from the main partition column will give a positive detector response; the material is then partitioned on the second column, after which the gas stream is deflected to the mass detector, by means of a two-way tap. Such a procedure could only deal with widely separated components, and the condition that $K \gg 1$ must be satisfied. An alternative method which would be satisfactory for multi-component mixtures is to trap all components on the adsorption column, and after completion of the run, place this column in front of the partition column, in a chamber sufficiently hot to quantitatively desorb all material; the run is repeated using the mass detector in place of the flame thermocouple detector.

EXPERIMENTAL

The molecular weights of a number of materials have been determined using the Martin gas density balance in series with the mass detector. Operating conditions are given in Table II.

The linearity of response of the gas density balance toward each sample was checked by covering a reasonable concentration range and plotting graphs of detector response (peak area) against the mass detector response (weight adsorbed). The molecular weight can be calculated from the slopes of the curves, since the slope gives A/q (eqn. 1) directly. However, more precise values can be obtained by calculating the mean value of A/q.

Several two-component mixtures were analysed, and the molecular weight

TABLE II

OPERATING CONDITIONS

Apparatus	Shandon KG2
Carrier gas	Nitrogen
Analytical gas flow rate	51 ml min^{-1}
Reference gas flow rate	51 ml min^{-1}
Gas density balance filament current	1.9 A
Sensitivity	$\times 10^3$
Mass detector ranges	1–5 mg

of each component calculated assuming that the remaining component was the standard. The molecular weight values given in Table III are the mean of about ten determinations. Bias values are given in terms of molecular weight, and not as percentage error.

TABLE III

MOLECULAR WEIGHT DETERMINATIONS (GAS DENSITY DETECTOR)

Compound	*Mean molecular weight*	*Standard deviation*	*True molecular weight*	*Bias*
Water[a]	17.5	—	18.0	— 0.5
Ethyl alcohol	43.8	—	46.1	— 2.3
Water[a]	18.0	0.13	18.0	zero
Ethyl alcohol	46.1	0.63	46.1	zero
Methyl alcohol[b]	> 28	—	32.0	*ca.* — 2
Ethyl alcohol	52.9	—	46.1	+ 5.8
Ethyl alcohol[c]	45.2	0.61	46.1	— 0.9
n-Propyl alcohol	62.3	1.70	60.1	+ 2.2
n-Propyl alcohol[c]	59.1	3.27	60.1	— 1.0
n-Butyl alcohol	75.9	6.06	74.1	+ 1.8
Isopropyl alcohol[d]	59.4	4.67	60.1	— 0.7
Nitromethane	61.8	5.22	61.0	+ 0.8
n-Propyl alcohol[e]	59.7	3.03	60.1	— 0.4
Methyl *n*-propyl ketone	87.1	6.35	86.1	+ 1.0
n-Butyraldehyde[e]	70.8	7.29	72.1	— 1.3
Methyl ethyl ketone	73.4	4.65	72.1	+ 1.3
Isopropyl alcohol[d]	60.4	—	60.1	+ 0.3
n-Propyl alcohol	59.8	—	60.1	— 0.3
Benzene[d]	76.5	2.41	78.1	— 1.6
Toluene	94.7	4.57	92.1	+ 2.6
n-Heptane[f]	90.9	15.23	100.2	— 9.3
n-Octane	128.4	24.25	114.2	+ 14.2
n-Heptane[d]	107.6	—	100.2	+ 7.4
n-Nonane	144.2	—	128.5	+ 15.7
n-Octane[f]	98.6	23.24	114.2	— 15.6
n-Nonane	159.8	29.75	128.5	+ 31.3

[a] Column D at 70°. (For column details, see Table VI.)
[b] Column E at 70°.
[c] Column D at 140°.
[d] Column E at 101°
[e] Column E at 68°.
[f] Column H at 106°.

The variations of bias and standard deviation with molecular weight are shown in Figs. 2 and 3 respectively. Clearly, accuracy and precision are inadequate over a molecular weight of about 100. In the region of 100, values are as good as those obtained by LIBERTI *et al.*[5], and become progressively better as molecular weight decreases.

For a relative composition analysis using the gas density balance, the molecular

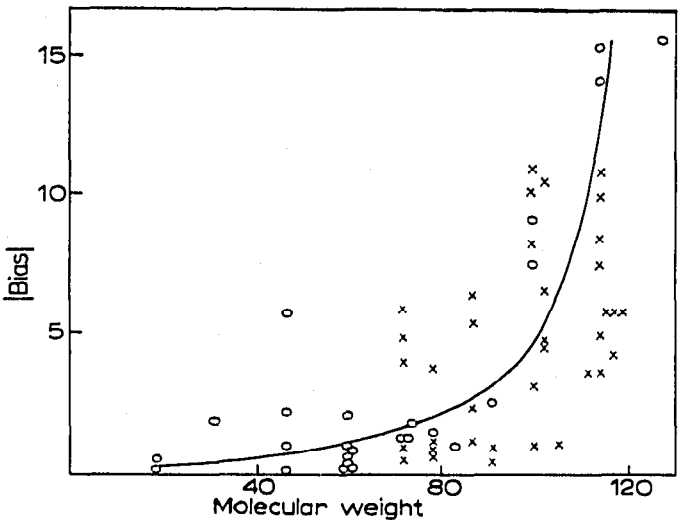

Fig. 2. Variation of bias with molecular weight. O, two-component mixtures; ×, multicomponent mixtures. For column details, see Table VI.

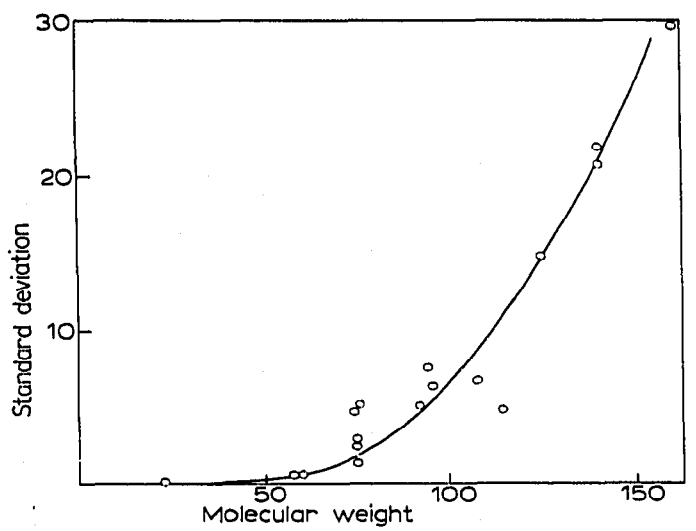

Fig. 3. Variation of standard deviation with molecular weight.

TABLE IV

ANALYSIS OF FATTY ACID MIXTURE

x_0 = true % composition; $\bar{x}_M$ = observed % composition using mass detector; $\bar{x}_D$ = observed % composition using gas density balance.

Compound	*Observed molecular weight*	*Monomer mol. wt.*	x_0	$\bar{x}_M$	$\bar{x}_D$
Water (standard)	18.0	18.0	—	—	—
Formic acid	54.8	46.0	—	—	—
Formic acid	54.8	46.0	62.04	60.79	56.74
Acetic acid	82.2	60.0	37.96	39.21	43.26

'eight of the components of the mixture must be known. The analysis of mixtures ontaining free fatty acids cannot be carried out using correction factors based on mple molecular weights, since the lower members of the series dimerise. The degree f dimerisation is dependent on temperature and pressure, so that the correction actors will depend on the conditions under which the analysis is carried out. The olecular weight of formic acid was estimated using water as a standard, and under he same conditions the percentage composition of a formic acid–acetic acid mixture vas calculated. The results are given in Table IV.

'ABLE V

IOLECULAR WEIGHT DETERMINATIONS (GAS DENSITY DETECTOR)

Compound		*True molecular weight*	*Mean detected molecular weight*				
			1	*2*	*3*	*4*	*5*
Cyclohexane	1	84.2	—	82.9	86.7	105.6	
Dichloroethylene	2	97.0	98.9	—	102.7	132.9	
n-Octane	3	114.2	109.3	106.9	—	154.8	
Carbon tetrachloride	4	153.8	108.9	106.5	113.6	—	
Benzene		78.1	—	78.9	79.2		
Toluene		92.1	91.0	—	92.5		
Ethyl benzene		106.2	103.7	105.1	—		
Methyl ethyl ketone		72.1	—	77.0	72.6		
Methyl *n*-propyl ketone		86.1	79.8	—	80.5		
Methyl *n*-butyl ketone		100.2	99.1	110.4	—		
Methyl ethyl ketone		72.1	—	71.2	65.7	68.1	69.1
Benzene		78.1	79.3	—	71.2	74.3	75.6
Ethyl acetate		88.1	102.7	100.5	—	93.5	75.8
n-Heptane		100.2	111.3	108.7	94.0	—	103.0
n-Octane		114.2	125.0	121.6	102.9	110.8	—
Ethyl acetate		88.1	—	93.8	90.5		
n-Propyl acetate		102.1	95.3	—	98.2		
n-Butyl acetate		116.2	111.9	122.0	—		
Ethyl acetate		88.1	—	82.1	79.8		
n-Propyl acetate		102.1	112.8	—	98.3		
n-Butyl acetate		116.2	138.6	122.0	—		
Butylene oxide		72.1	—	63.4	66.1		
Dioxan		88.1	110.8	—	94.8		
n-Octane		114.2	140.4	104.1	—		

TABLE VI

COLUMN DETAILS

Reference	*Stationary phase*		*Inert support*		*Length* (*m*)	*I.D.* (*mm*)
	Type	%	*Type*	*B.S. Mesh*		
D	Porapak Q	—	—	100–120	0.56	3
E	PEGA	20	Chromosorb G	72–85	4	4
H	ApL	20	Chromosorb G	72–85	2	4

The mass detector gives excellent quantitative results, but the gas density balance results are only fair.

An advantage of the determination of molecular weights by gas chromatography is that pure isolated materials are not required. The analysis of multi-component mixtures represents a more realistic situation than the analysis of a two component mixture in which one material is the added standard. For the multi-component mixtures listed in Table V each component in turn was taken as the standard, and the mean molecular weight of all the remaining constituents calculated. Thus for an n-component mixture, there will be n standards and $(n-1)$ values for the mean molecular weight of each component. It is not valid to calculate the mean of the $(n-1)$ molecular weights, to give a single value, since the different standards used to calculate the values all have different molecular weights themselves, and hence fall on different parts of the curve shown in Fig. 1.

The variation of bias with molecular weight is shown in Fig. 2. Details of the columns used in this work are given in Table VI.

CONCLUSIONS

By operating the gas density balance and mass detector in series, satisfactory molecular weight values may be obtained for materials within a given molecular weight range. The range is determined by the molecular weight of the carrier gas. Using nitrogen as carrier, satisfactory molecular weights were obtained over the range 18 to 100, for both two-component mixtures and multi-component mixtures.

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