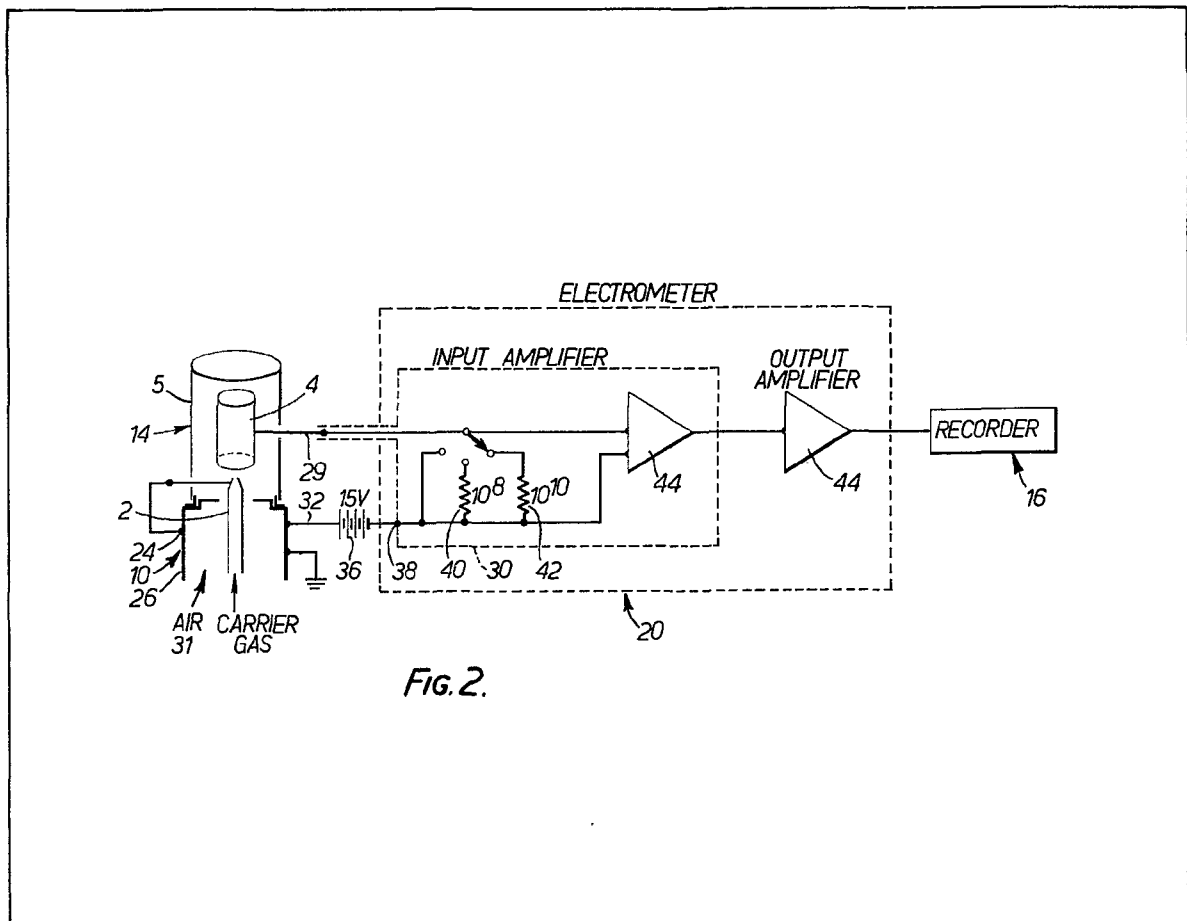


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(54) **Radio gas chromatography**

(57) Apparatus for monitoring compounds labelled with highly radioactive tritium, ¹⁴C or similar molecules includes a gas-liquid chromatograph column, a variable post-column splitter, a flame ionisation detector connected to receive a minor proportion of the output of the splitter, an ion chamber (10) connected to receive a major proportion of the output of the splitter, a differential electrometer connected to the flame ionisation detector, an electrometer (20) capable of measuring currents of the order of 10⁻¹² amps at full scale deflection connected to the ion chamber and recording means (16) connected to the electrometers.



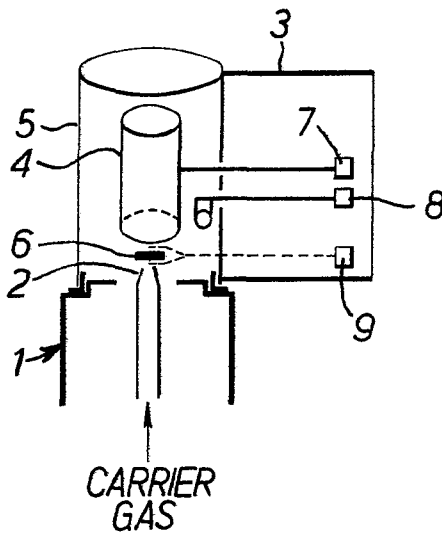


FIG. 1.

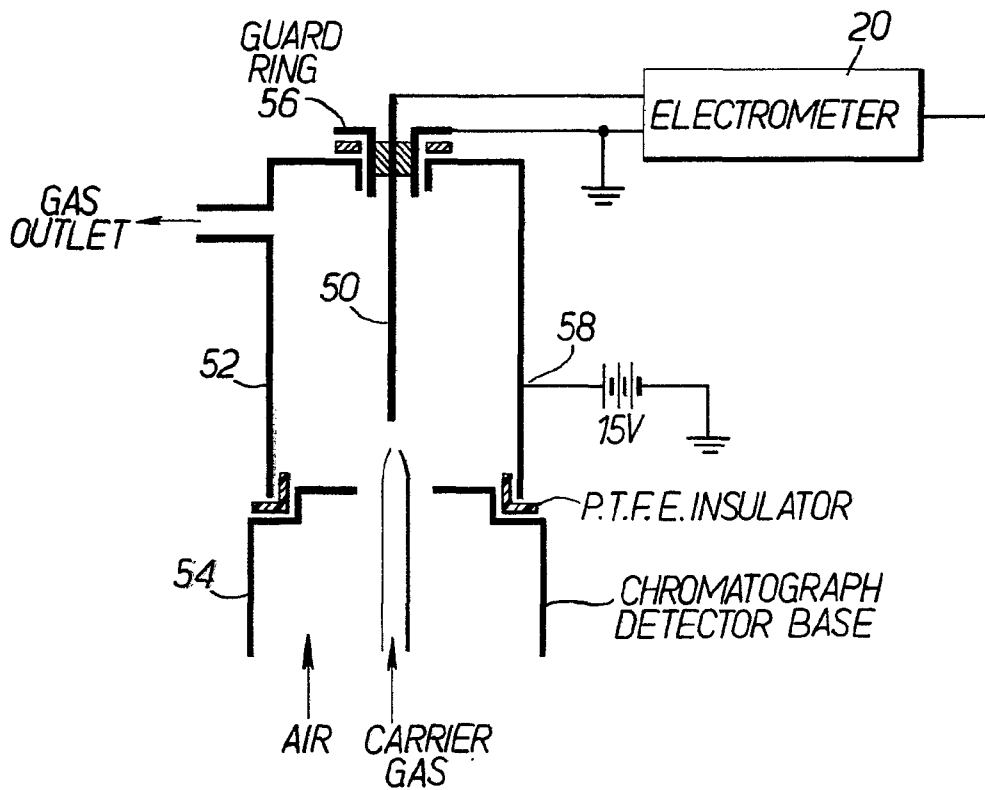


FIG. 4.

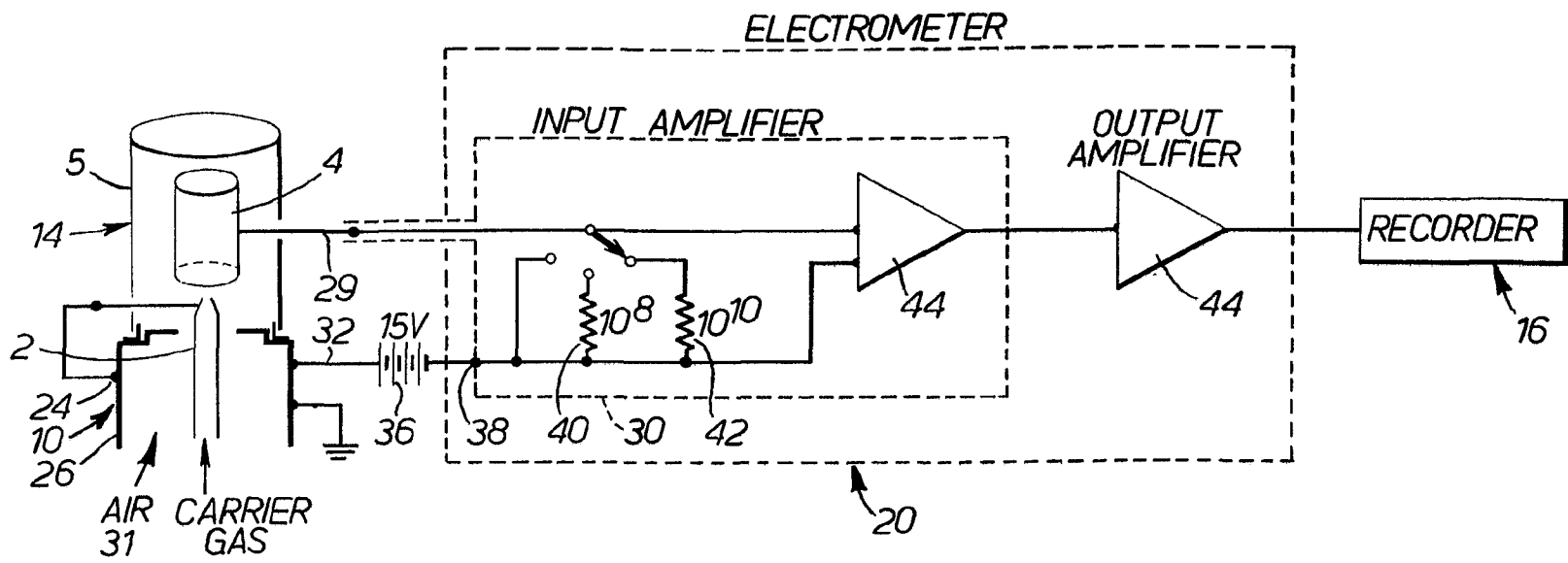


FIG. 2.

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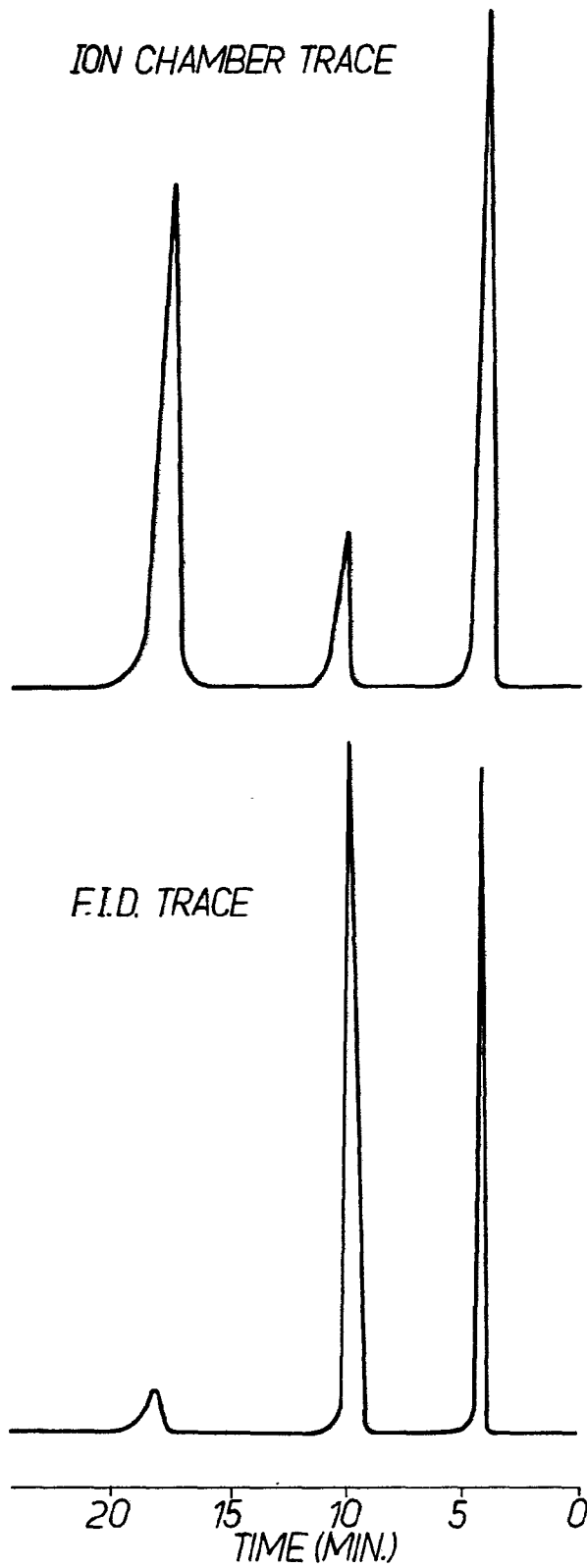


FIG. 3.

SPECIFICATION

Radio gas chromatography

5 This invention relates to radio gas chromatography.

The rapid estimation of tritium (^3H) among the components of mixtures of radio-active labelled compounds of sufficient volatility can be achieved

10 by the conventional technique of radio-gas-liquid chromatography. Instruments have already been developed for such methods of analysis and examples of instruments have been reviewed in the Journal of Chromatography 1976, 127, by M.

15 Matucha and E. Smolkovae. These instruments are also reviewed by T. R. Roberts in Radio Chromatography – "The Chromatography and Electrophoresis of Radio-Labelled Compounds" published by Elsevier, Amsterdam 1978. These methods

20 and instruments have been specifically developed with the purpose of achieving maximum sensitivity for compounds of low specific radioactivity.

The development in 1978 of ^3H nuclear magnetic resonance spectroscopy as described for example in

25 "Tritium Nuclear Magnetic Resonance Spectroscopy" published in "Isotopes in Organic Chemistry" edited by E. Bunce and C. C. Lee and published by Elsevier, Amsterdam 1978, 4 ch.1 provides a method

30 for the determination of the position of tritium in molecules and in turn this has created a need for the radio-chemical analysis of mixtures with components of high specific radioactivity. Typically, samples containing 10-30 mCi of radioactivity in volumes of the order of 0.05 ml can be prepared for ^3H nuclear

35 magnetic resonance analysis use in studies such as surface catalysis or biosynthesis (see J. L. Garnett, M. A. Long and C. A. Lukey in the Journal of The Chemical Society, Chem. Commun. 1979, 634 and also J. A. Elvidge, D. K. Jaiswal, J. R. Jones and R.

40 Thomas, Journal of The Chemical Society, Perkin II, 1977, Page 1080). Such high radioactivity samples should permit detection without recourse to the more complex and thus expensive methods based on proportional, scintillation, or solid state detector

45 systems. It is now proposed to provide a modified dual detector gas chromatograph which is capable of monitoring highly radioactive tritium and similarly-labelled molecules such as ^{14}C labelled compounds.

50 According to the present invention there is provided apparatus for monitoring compounds labelled with highly radioactive tritium, ^{14}C or similar molecules comprising a gas-liquid chromatograph column, a variable post-column splitter, a flame ionisation

55 detector connected to receive a minor proportion of the output of the splitter, an ion chamber connected to receive a major proportion of the output of the splitter, a differential electrometer connected to the flame ionisation detector, an electrometer capable of

60 measuring currents of the order of 10^{-12} amps at full scale deflection connected to the ion chamber and recording means connected to the electrometers.

The invention will now be described, by way of example only, with reference to the accompanying diagrammatic drawings, in which:

65 Figure 1 is a diagram illustrating a commercially available flame ionising detector forming a part of a dual detector gas chromatograph;

70 Figure 2 is a circuit diagram of a flame ionisation detector modified to act as an ion chamber and an electrometer forming parts of an apparatus in accordance with the invention;

75 Figures 3a and 3b are graphs plotting the ion chamber trace and the flame ionisation detector trace against time for a typical sample of mixed tritium hydrocarbons; and

80 Figure 4 is a circuit diagram of a modification of the circuit of Figure 2 in which the flame ionisation detector is replaced by an ionisation chamber.

In a flame ionisation detector the electrical conductivity of the flame, which depends on its combustion provides the basic measurement parameter. This conductivity is a function of hydrogen flow, carrier gas flow rate, temperature, and the bleed rate of the associated chromatographic column.

85 The hydrogen flow is adjusted to give maximum combustion efficiency and hence maximum conductivity for the condition obtaining at any given instant. A connection is provided for an electrical potential, producing a standing current which excites the flame and which is collected at the input of the electrometer connected to the detector. This standing current should be properly compensated in order to zero set the electrometer output signal.

90 When the organic components, eluted from an associated chromatographic column, burn in the flame, the electrical conductivity changes with consequent current variation.

95 The electrometer amplifies these currents and generates proportional electrical signals which are recorded on a recorder chart as peaks and constitute the analysis chromatogram.

100 The flame ionisation detector comprises a stainless steel base body 1, a flame jet 2 and a detector cell 3. A collector electrode 4 disposed centrally within an aluminium combustion chamber 5 consists of a 10 mm. diameter cylinder. A fork contact electrically connects a polarisation electrode to a potential source. An automatic flame igniter 6 is located adjacent to flame jet 2. The electrodes and the automatic igniter are electrically connected by connectors 7, 8 and 9 to the electrometer.

105 The gas chromatograph used as a basis for apparatus in accordance with the invention comprises two identical flame ionisation detectors, a variable post-column splitter, a dual pen recorder and electrometer of single different type. This apparatus is manufactured in Italy by Carlo Erba Strumentazione (a company of the Montedison Group). One of the flame ionization detectors is replaced by an ion chamber which may be physically based on the flame ionisation detector. This ion chamber is connected to a second electrometer capable of measuring currents of the order of 10^{-12} amps at full scale

deflection. A vibrating reed instrument is suitable for this purpose.

The ion chamber 10 forming part of the gas chromatograph has the following modifications in comparison with a standard flame ionisation detector. Unmodified parts have been given the same reference numerals.

1. The connector 8 to provide a flame polarising potential is omitted or disconnected;

2. The input socket to the flame jet 2 is grounded at 24 to the outer case 26;

3. The connection 9 to the igniter terminal of the flame ionisation detector is omitted;

4. The signal connector is removed from the cylindrical collector electrode 4 socket of the flame-ionising detector and replaced with a short length of low capacitance, co-axial cable 29 so as to connect the cylindrical collector electrode 4 to the input amplifier 30 of the vibrating reed electrometer 20;

5. The post-column splitter (not shown) is so arranged that 10% of the carrier gas from the column is passed to the flame ionising detector (not shown) and 90% to the ion chamber 10; and

6. The second flame-ionising detector 10 is operated as an ion chamber with no hydrogen flow but with approximately a normal air flow at 31 to act as a purge gas.

To provide for ion chamber operation of the second flame ionising detector 10 a connection 32 is provided to a polarising potential for example provided by a dry cell battery 36 connected between the grounded outer case 26 of the ion chamber and an input screen 38 of the input amplifier 30 of the electrometer 20. The electrometer input circuit permits elevation with respect to ground of its input stages by at least the magnitude of the polarising voltage. In addition to the input amplifier, the electrometer also includes an output amplifier 44 the output of which is connected to a recorder 16.

Tests have shown that a 15 volts polarising potential provided by battery 36 is adequate to obtain the necessary saturation current within the ion chamber 10.

The operation of the gas chromatograph will now be described. The ion current is collected between the cylindrical collector electrode 4 of the ion chamber 10 and its outer case. This current is measured as a voltage drop in the range 10mV to 1000mV across an input resistor 40, 42 in the corresponding electrometer which would be selected in the range 10^8 to 10^{10} ohms.

A test injection of 1 microlitre of a sample of benzene with a specific radioactivity of 1 millicurie/microlitre gave a peak signal of the order of 1000mV with the 10^{10} ohm resistor 42 selected, the precise signal height being dependent on the spread of the emerging sample and flow rate of the air purge gas through the ion chamber. This response corresponds approximately to 10% of the sample resident in the sensitive region of the ion chamber at the signal peak if complete ion collection is assumed.

The flow rate of the purge gas (air) will normally be chosen such that sensitivity will remain adequate and there will be no significant loss of resolution of

components within the volume of the ion chamber. Ion chambers are subject to slight changes in efficiency when the gas composition is modified by the components emerging in the effluent of the chromatograph column. This phenomenon will be reduced in importance when sample radioactivities are sufficiently high to allow for increased purge gas flow rates without decreasing the sensitivity limit of the chamber below the sample radioactivity.

As hereinbefore described the gas chromatograph and the method of use enables the simultaneous recording of chemical concentration and radioactivity of components emerging from a chromatograph column as illustrated in the graphs of Figure 3.

Radioactivity of high specific radioactivity materials can be measured which has not hitherto been possible at reasonable cost with other methods and apparatus.

Where even higher sensitivity is required, the electrode and case assembly of the second flame ionisation detector of the gas chromatograph may be replaced by a specially constructed chamber fitting the base of the flame ionising detector of the chromatograph. This modification is illustrated in Figure 4. The ion chamber 10 then has a single rod 50 acting as a central electrode and a cylindrical chamber 52 which is electrically insulated from the detector base 54. A guard ring 56 around the central electrode 50 permits the use of a higher sensitivity electrometer in association with a 10^{12} ohm input resistor. Electrical leakage paths will be reduced with this construction and the electrometer would operate with input return at ground potential since the polarising potential will be applied to the outer chamber wall as indicated at 58 in Figure 4.

Both the ion chambers hereinbefore described enable tritium assay with the advantage that outlet stream combustion and reduction tubes used in conventional proportional counter methods for gas chromatography tritium analysis are not necessary. The instrument can be rapidly energised without the need for packing and heating of silica combustion tubes which themselves frequently introduce memory effect problems and high radioactive background due to inadequate operation. Further, where purification of a compound is the objective, the method and apparatus hereinbefore described are advantageous for adaption to a preparative scale gas chromatograph.

While the method and apparatus hereinbefore described is particularly intended for analysis of tritium-labelled compounds it is also applicable to ^{14}C -labelled compounds and will be applicable to analysis of other compounds with other highly radioactive labels.

The main embodiment employs in a radio gas chromatograph an ion chamber which is physically an adaptation of an existing flame ionisation detector. The modification of Figure 4 indicates that even higher sensitivity can be achieved with further changes and it is possible that an ion chamber constructed specifically as such will provide even better results.

Pen recorders are preferred because of their low cost, but it will be understood that other convention-

al recorders can also be used.

CLAIMS (filed 9/3/82)

1. Apparatus for monitoring compounds labelled
with highly radio-active tritium, ^{14}C or similar mole-
5 cules comprising a gas-liquid chromatograph col-
umn, a variable, post-column, splitter, a flame
ionisation detector connected to receive a minor
proportion of the output of the splitter, an ion
chamber connected to receive a major proportion of
10 the output of the splitter, a differential electrometer
connected to the flame ionisation detector, an
electrometer capable of measuring currents of the
order of 10^{-12} amps at full scale deflection con-
nected to the ion chamber, and recording means
15 connected to the electrometers.

2. Apparatus according to claim 1 wherein the
ion chamber comprises jet defining means for
admitting the major proportion of the output of the
splitter surrounded by an air inlet casing, a chamber
20 arranged to receive the jet and a cylindrical collector
electrode, the jet defining means being electrically
grounded to the air inlet casing and the collector
electrode being connected by a co-axial cable to the
input of the ion chamber electrometer.

3. Apparatus according to Claim 1, wherein the
ion chamber comprises jet defining means for
admitting the major proportion of the output of the
splitter, surrounded by an air inlet casing, a cylin-
drical chamber mounted on the air inlet casing and
30 having a gas outlet and a central rod electrode
disposed in alignment with the longitudinal axis of
the jet defining means and connected to the ion
chamber electrometer, means for applying a positive
potential to the cylindrical chamber and means
35 serving to insulate electrically the air inlet casing
from the cylindrical chamber.

4. Apparatus according to any one of the preced-
ing claims, wherein the ion chamber electrometer is
a vibrating reed instrument.

5. Apparatus according to any one of the preced-
ing claims wherein the recording means is a dual
pen recorder.

6. Apparatus for monitoring radioactive labelled
compounds substantially as hereinbefore described
45 with reference to Fig. 2 or Fig. 4 of the accompanying
drawings.