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PARALLEL FLAME IONIZATION DETECTION–TOTAL ION CURRENT RECORDING IN CAPILLARY GAS CHROMATOGRAPHY–CHEMICAL-IONIZATION MASS SPECTROMETRY

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SUMMARY

The need for independent dual detection in the analysis of complex mixtures by gas chromatography–chemical-ionization mass spectrometry is illustrated. Monitoring of the gas chromatographic effluent by means of universal detection and unaltered uniform response by flame ionization detection is a desirable supplement to the customary, highly selective, monitoring of the total ion current, especially in consecutive analyses of the same sample, where the chemical-ionization reagent gas is varied. Since the gas chromatograms obtained by flame ionization detection are unaffected by changes in chemical-ionization conditions, they provide a safer common basis for interrelating spectral data from successive runs than do the total ion current records. For the special case of reconstructed gas chromatograms generated by computers from digitized total ion current values, direct correlations are conveniently achieved by calibrating both the flame ionization detection and total ion current records in spectrum index numbers through the use of an event marker, triggered by the data system.

INTRODUCTION

The combination of high-efficiency gas chromatography with chemical-ionization mass spectrometry (GC–CIMS) appears to offer a promising new approach for the determination of the structures of unknown compounds present in complex mixtures which resist the isolation of pure materials. The potential of this method was realised when it was found that the use of more than one chemical-ionization (CI) reagent could result in new, complementary, structural evidence and thus provide a means of selective probing of certain structural features**. Convenient variation of the GC–CIMS experiment on the same sample by changing the reagent gas became possible through dual-gas interfacing, gases other than the GC carrier gas being employed and freely selected[3–5]. By the use of such equipment, the reagent gas is not

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** For recent reviews of the reagent gases in current use see refs. 1 and 2.

admixed to the GC effluent before entering the ion source of the mass spectrometer, and thus the carrier gas and, consequently, the GC conditions can be kept unchanged throughout a series of runs. As a first benefit, directly comparable GC traces can be obtained simply by total ion current (TIC) monitoring, at least as far as the retention times are concerned. In many cases this will secure a sufficiently broad basis for an immediate correlation of the results although they are obtained under widely differing CI conditions.

Difficulties with this mode of single detection may, however, arise when exactly analogous data of poorly resolved components have to be compiled from the various runs and correlated throughout the series of experiments. Usually, this will involve selecting, from a set of spectra in a given run, the most representative scan of the component of interest, and locating the latter, as accurately as possible, within a GC peak pattern of the TIC chromatogram. This will determine the position of the spectrum on the time axis of a two-dimensional mass–time data field. The next step will aim at finding exactly corresponding positions within the TIC chromatograms of all other CI runs. This will ensure that only those spectra are correlated which correspond to identical, or at least very similar, retention indices[6] and thus reflect comparable concentrations of the constituent in question. This step may also be viewed as the retrieval of a time-coherent two-dimensional subset of data along the CI reactant axis from a three-dimensional mass–time–reactant array of mass spectral data.

In spite of the fact that the retention times remain largely unchanged during a series of CI experiments, locating of the most representative spectra of an unresolved component on a purely visual basis, *i.e.*, comparing analogous GC peak patterns in the TIC traces, is likely to be difficult for several reasons. Under varying CI conditions, the intensity profiles of unresolved GC peak dusters can vary considerably from run to run, rendering them sometimes past recognition. Marked changes of profile are even common when the sample is heterogeneous with respect to the classes of compounds of which it is composed. In such cases, the differences in the proton affinities between the substrate and reagent gas may become too small to allow efficient protonation of some constituents, *i.e.*, CI will discriminate heavily against them especially when mildly acidic reagent gases are employed. Unfortunately, these highly selective reactants are the very ones which have to be chosen for attempts at a differential analysis of the special structural features that are hard to detect by other mass spectroscopic methods[1,2].

Other problems of single CI–TIC recording, posed by instrumentation rather by than gas phase ion chemistry, relate to the sharp demarcation of the TIC of the sample and reactant, which is not always easily attained. Mildly acidic reagent gases, which are frequently quite polar, tend to form oligomeric cluster ions of the type $(H–X)_nH^+$ ($n = 2$–4), in relative abundances that are not only sensitive towards changes in source conditions but which may also extend into mass ranges commonly occupied by sample ions to be collected in TIC recording. Since the abundances of reactant ions generally exceed those of sample ions by some orders of magnitude, they must be rigorously excluded from TIC recording in order to attain acceptable sensitivity. When quadrupole mass spectrometers are used, this can be conveniently achieved by integrating mass-resolved ion currents over pre-set limited mass ranges and cutting off lower portions which contain reactant but no sample ions (*e.g.*,

when using methane or isobutane, the TIC is usually sampled above *m/e* 60). With polar reagents like methanol or small aliphatic amines, cluster ions will, however, extend even beyond *m/e* 100, thus interfering with the mass range to be taken as representative of the compound to be analyzed. With data systems, the digitized mass-resolved TIC can be recorded with deletion of sets of specified *m/e* values, thus permitting deliberate exclusion of such contributions provided that no overlaps occur. The use of labelled reagent gas (*e.g.*, [$^2H_4$]methanol instead of CH_3O^2H) may have to be considered if overlap occurs.

Besides the potentially large disparities in peak shapes of the unresolved components due to discriminatory CI response, small differences in the absolute positions along the time coordinate may add to the uncertainty in visual correlation of TIC traces of complex mixtures. These minor deviations in retention times naturally arise from the lack of exact reproducibility in practical work in the GC part of the experiment, in spite of the efforts to keep the parameters constant. Unfortunately, the feasibility of correlating spectral data via unaffected retention indices rather than retention times is similarly impaired by the pronounced selectivity of the CI response. With most gases of interest, other than methane, the internal standards for index measurements, usually homologous *n*-paraffins, are not ionized at all.

One simple way of overcoming these problems of correlation experimentally is by splitting the GC effluent and feeding a portion of it into a universal rather than a selective independent detector, run in parallel to the TIC-recording mass spectrometer. The flame ionization detector (FID), often used in electron-impact GC–MS (GC–EIMS) systems[7–9] for various other reasons, is the obvious device of choice. It exhibits a largely uniform response to widely differing organic substrates, and is sufficiently sensitive to produce signal amplitudes which are comparable to those obtained by TIC recording. FID gas chromatograms, now identical in both dimensions, *i.e.*, retention time and concentration amplitude, will be produced in successive runs irrespective of which reagent gas is used. The details of the design and performance of such a dual-recording GC–CIMS systems are given below.

EXPERIMENTAL

Fig. 1 shows a schematic diagram of the capillary GC–CIMS system used in our laboratory for GC–EIMS and multiple GC–CIMS analyses of mixtures, and which is equipped with provisions for rapid switching of the reagent gases. The main components of the system are a Carlo Erba Fractovap 2101 AC capillary gas chromatograph (a), a Finnigan 3300 mass spectrometer (i) and a Finnigan 6000 interactive data system (j). It also incorporates an effluent splitter (d) with *ca.* 1:1 splitting ratio, a conventional hydrogen FID (e), a coaxial dual-gas GC–CIMS interface (g, h)[5] and a pair of vaporizers (p–r, of which only one is depicted in the scheme) for liquids to be used as CI reagent gases. The splitting device (d), manufactured from glass and platinum capillaries according to Etzweiler and Neuner-Jehle[10], is placed in the GC oven and feeds a portion of the effluent to the FID (e) as the universal detector. By use of a *ca.* 1:1 splitting ratio, it was not necessary to add a make-up gas in order to prevent losses in resolution due to the dead volume of the connecting capillary lines.

The two vaporizers for liquid reactants can be operated independently through assemblies of regulating and simple shut-off valves (n and o, respectively). The heated

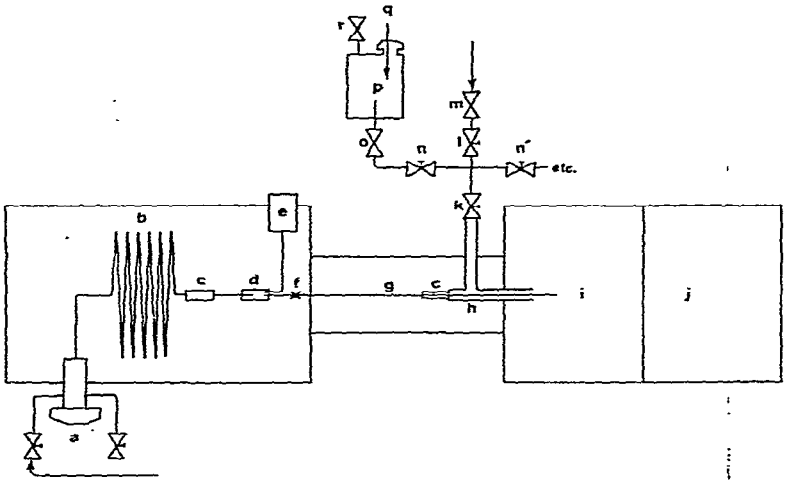

Fig. 1. Schematic diagram of the dual-recording capillary GC–CIMS–computer system equipped with an effluent splitter, vaporizers for liquid reactants and coaxial dual-gas interface. Components: (a) Fractovap 2101 AC gas chromatograph with Grob-type injector, (Carlo Erba, Milan, Italy); (b) Emulphor-ON 870 glass capillary column (50 m × 0.35 mm) (H. and G. Jaeggi, Trogen, Switzerland); (c) polyimide ferrule, Vespel SP-1 (Dupont, Genève, Switzerland); (d) splitting device, glass and platinum capillaries[10]; (e) hydrogen FID (Carlo Erba); (f) platinum restriction; (g, h) coaxial dual-gas interface; (g) interface capillary, AR-glass (0.9 mm O.D., 0.3 mm I.D., pre-treated according to ref. 11; (h) stainless-steel reactant gas line (3.2 mm O.D., 1.2 mm I.D.) (*cf.* ref. 5); (i) Finnigan 3300 mass spectrometer; (j) Finnigan 6000 interactive data system; (k, l, n) SS-4BMG bellows metering valves, (Nupro; Kontron, Zürich, Switzerland); (m, o, r) 4172G2Y bellows shut-off valves (Hoke; Mathemie, Therwil, Switzerland); (p) stainless-steel vessel, 200 ml; (q) silicon rubber septum.

200-ml vessels (p) are charged with liquids (*ca.* 5 ml) by means of injection by syringe via silicon-rubber septa (q), or discharged by applying a reduced pressure to the vent valves (r). The vessels may also be used as expansion volumes for gases like NH_3, for which constant flow is hard to maintain when supplying them directly from a pressure cylinder through the main reagent gas line (k–m). For measurements, 1-μl samples of a 0.1 % solution were injected without stream-splitting while maintaining the column temperatures at *ca.* 50°. The column temperature was programmed after an initial period (3 min) from 50 to 200° with a gradient of 2°/min. Helium was supplied as carrier gas at a pressure of 1.6 bar. The interface temperature was maintained at 260°.

For CI operation, reagent gases of the highest available purity were employed: methane and isobutane (L'Air Liquide, Genève, Switzerland, types N 55 and CH 35, respectively); ammonia (Fluka, Buchs, Switzerland; purissimum); CH_3O^2H (Ciba-Geigy, Basel, Switzerland; > 99.5 atom % deuterium). Optimized CI conditions were secured by operating the source at pressures of 0.7–1 mbar (readings from an uncalibrated thermocouple gauge) with reagent: carrier-gas ratios of *ca.* 10:1. The filament current, electron energy and ion-source temperature were maintained at 200 μA, 150 eV and 140–150°, respectively.

Analog recording of the total ion current gas chromatograms (TIC–GC) required adjusting the electronically integrated mass ranges to the respective reagent

gas, *e.g.*, *m/e* 60–350 for methane and isobutane, or *m/e* 103–350 for CH_3O^2H, in order to exclude reactant-ion contributions. Alternatively, TIC traces were generated as reconstructed gas chromatograms (TIC–RGC) by use of the dedicated interactive data system (j), acquiring and storing CI mass spectra (for computing the digital TIC values) continuously during the analyses over specified mass ranges at selected scan rates. For example, for a CI(NH_3) run, a mass range of *m/e* 72–350 was chosen with integration times of 7 msec/a.m.u. In plotting these TIC–RGC records, spectrum index numbers rather than time equivalents were used for the calibration of the time axis. In order to allow direct correlations, this calibration scale was simultaneously transferred as a spectrum number (SN) trace on to the analog FID chromatogram (Perkin-Elmer Model 56 recorder equipped with an event marker, triggered by the SN generator of the data system), a pulse signal being supplied at suitable intervals, *e.g.*, at every fifth spectrum acquired. The complete spectra were inspected after the components had been located by means of the spectrum numbers from the TIC–RGC plots, or, more conveniently, by use of a cathode-ray tube (CRT) display (Hewlett-Packard, Type 1311 A) which allows the simultaneous observation of TIC–RGC and mass traces. The sequential inspection of a series of spectra, taken across the GC peak, permits a rapid search for the most representative scan for unresolved components.

RESULTS AND DISCUSSION

The performance of the system was tested by subjecting a synthetic mixture of approximately equal amounts of aliphatic and aromatic compounds, comprising 70 components, to a series of GC–CIMS experiments with different reagent gases. Besides saturated and unsaturated hydrocarbons, the mixture contained alcohols, ethers, halides, amines, esters, aldehydes and ketones. Only little deterioration of the GC resolution was observed for either mode of recording when compared to single detection by means of FID (GC alone) or TIC (GC–MS).

Some results obtained with this mixture are reproduced to illustrate the difficulties in correlating different CI runs as discussed above. Thus, Figs. 2–4 show the markedly differing CI–TIC gas chromatograms of runs with CH_4, $(CH_3)_3CH$ and CH_3O^2H, respectively, *i.e.*, with increasingly milder, and hence more selective, reactants (upper curves). The figures also display the uniform FID traces (lower curves) which were recorded in order to facilitate identification of the GC fractions in spite of the differing signal amplitudes. The assignments of the various components (*cf.* Table I; the numbers refer to the GC fractions) were, in the case of overlapping, arrived at on this basis, and were verified by analysis of the spectra recorded at appropriate instants during these runs.

Methane (Fig. 2), a strongly acidic and thus a rather universal protonating agent (CH_5^+ ions!), ionized and permitted detection of all of the components. Hence a record was produced which more closely resembles the FID chromatogram than those of the other reactant gases employed. In contrast, isobutane (Fig. 3) displayed, as expected on thermodynamic grounds, an essentially complete suppression of aliphatic hydrocarbons (components 1, 3, 10, 20, 26, 33 and 44), and moderate to severe discrimination towards aromatic hydrocarbons (*e.g.*, components 2, 4, 5, 8, 9, etc.). The CI–TIC trace of the analogous CH_3O^2H run (Fig. 4) showed the expected enhancement of this discriminatory effect, as well as its extention to additional com-

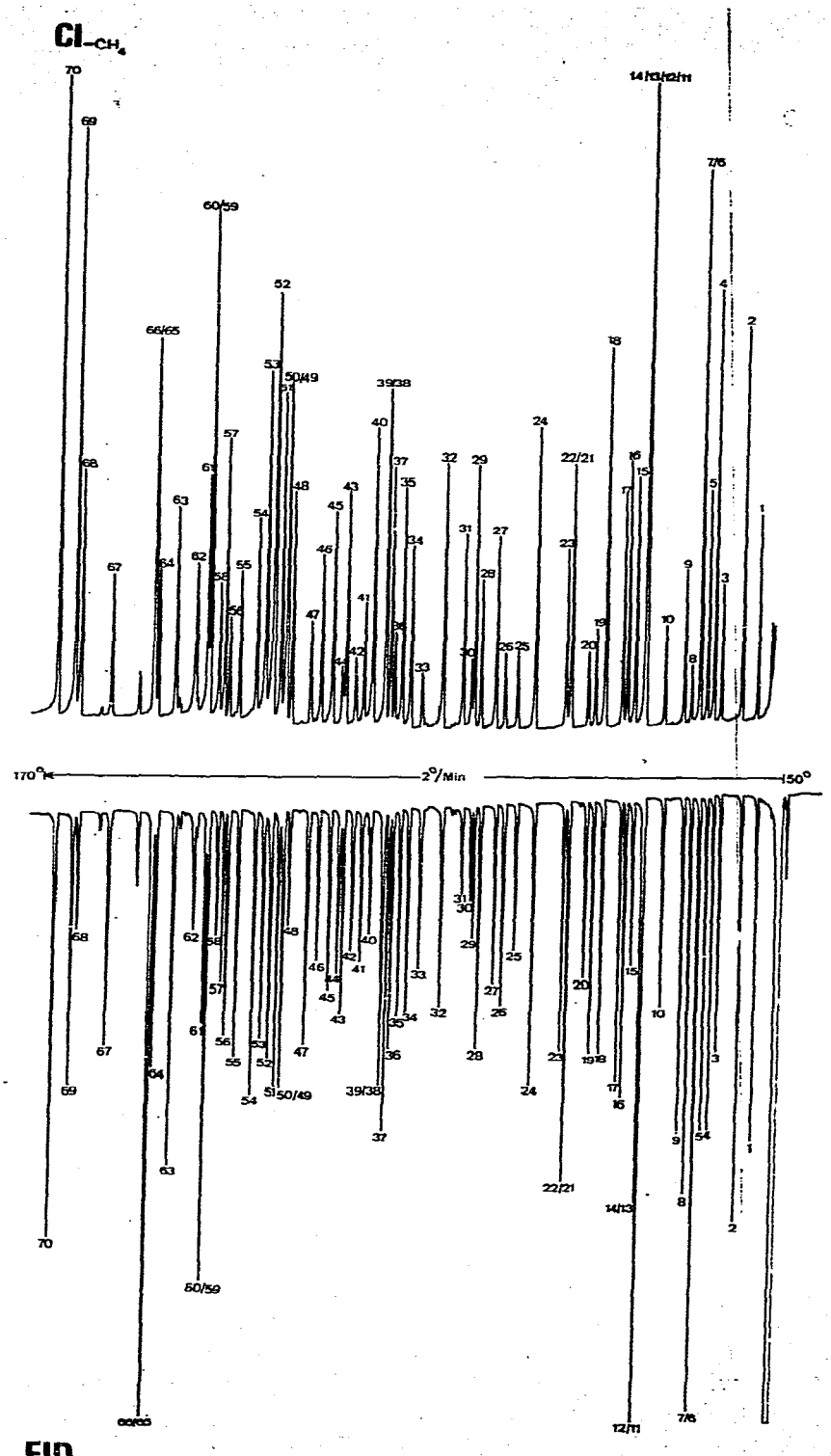

Fig. 2. Comparison of total-ion-current (upper trace, methane reactant) and flame-ionization detection (lower trace) for a synthetic mixture (*cf.* Table I). Glass capillary column (50 m × 0.35 mm) coated with Emulphor-ON 870. Mass range of analog TIC integration, *m/e* 60–350.

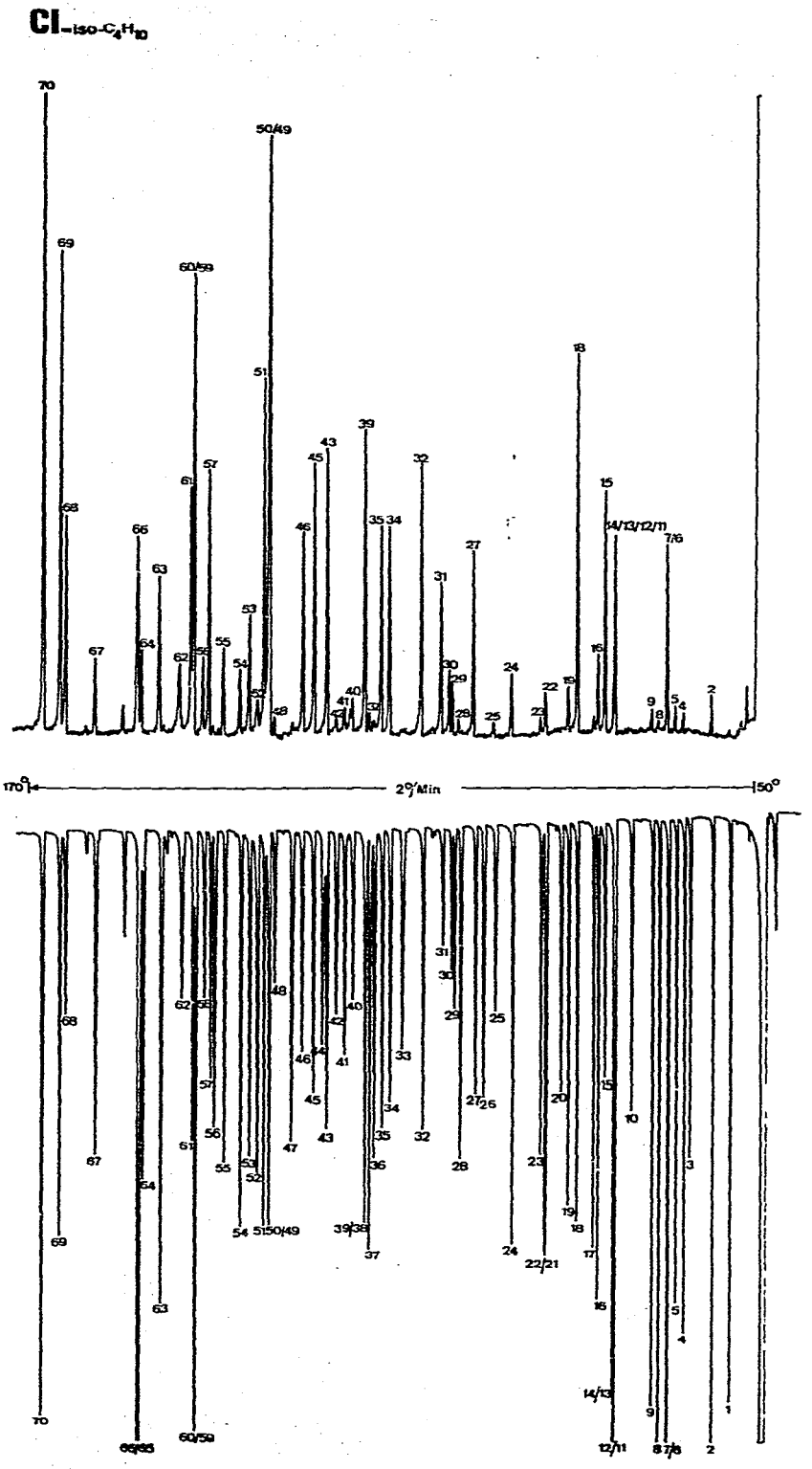

Fig. 3. Comparison of total-ion-current (upper trace, isobutane reactant) and flame-ionization detection (lower trace) for a synthetic mixture (*cf.* Table I). Details as in Fig. 1.

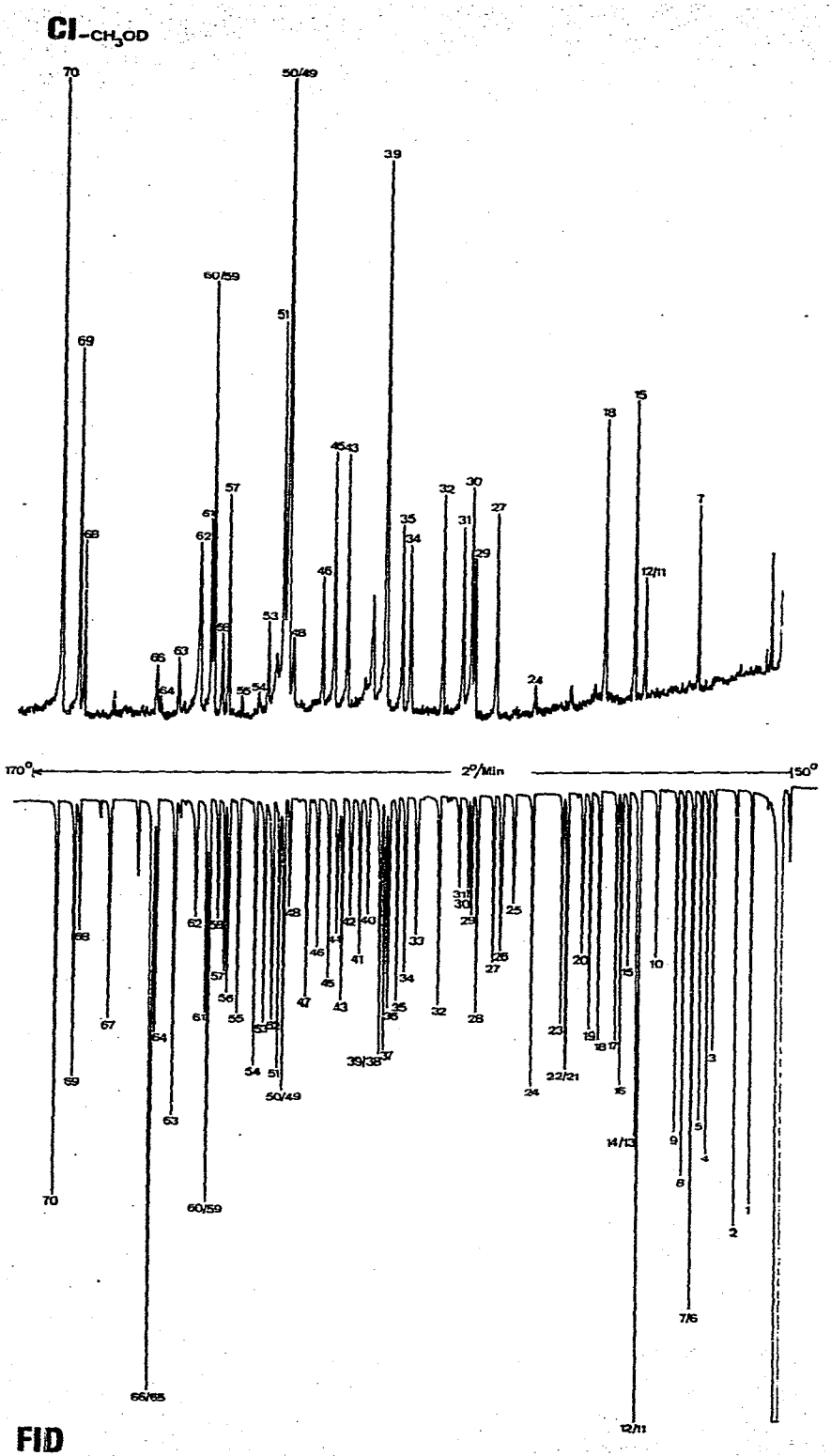

Fig. 4. Comparison of total-ion-current (upper trace, CH_3O^2H reactant) and flame-ionization detection (lower trace) for a synthetic mixture (*cf.* Table I). Column as in Fig. 1. Mass range of analog TIC integration, *m/e* 103–350.

TABLE I

IDENTITIES OF GC FRACTIONS 1–70 (INCREASING RETENTION VALUES) OF A SYNTHETIC MIXTURE

The fraction numbers correspond to those in Figs. 2–5.

No.	*Compound*	*No.*	*Compound*
1	*n*-Decane	36	*n*-Heptylbenzene
2	Ethylbenzene	37	Phenylcyclohexane
3	*n*-Undecane	38	2,6-Dichlorostyrene
4	Chlorobenzene	39	Diethyl succinate
5	*n*-Propylbenzene	40	1,5-Dibromopentane
6	4-Ethyltoluene	41	Naphthalene
7	1,8-Cineole	42	2-(*n*-Heptyl)-1-nonene*
8	*tert.*-Butylbenzene	43	2-Methylacetophenone
9	*sec.*-Butylbenzene	44	*n*-Hexadecane
10	*n*-Dodecane	45	4-Methylacetophenone
11	2-Methyl-3-phenyl-1-propene	46	4-Isopropylbenzaldehyde
12	Anisole	47	*n*-Octylbenzene
13	*n*-Butylbenzene	48	1,6-Dibromohexane
14	Bromobenzene	49	Nerol
15	6-Methyl-5-hepten-2-one	50	2-Bromobenzaldehyde
16	*tert.*-Pentylbenzene	51	2,6-Dimethylaniline
17	*sec.*-Pentylbenzene	52	2-Chlorophenol
18	Cyclohexyl methyl ketone	53	Benzyl alcohol
19	1-Phenyl-2-butene	54	1-Methylnaphthalene
20	*n*-Tridecane	55	1-Phenyl-1-heptyne
21	1,4-Diisopropylbenzene	56	*n*-Nonylbenzene
22	1,4-Dichlorobenzene	57	2-Chloroaniline
23	*n*-Pentylbenzene	58	Diethyl adipate
24	Coumarone	59	2-Ethylnaphthalene
25	2-(*n*-Hexyl)-1-octene*	60	2-Methoxybenzaldehyde
26	*n*-Tetradecane	61	2,6-Dichloroaniline
27	N,N-Dimethylaniline	62	2-Bromophenol
28	*n*-Hexylbenzene	63	1,3-Dimethylnaphthalene
29	1,4-Dibromobutane	64	1,4-Dimethylnaphthalene
30	4-Bromochlorobenzene	65	*n*-Decylbenzene
31	Diethyl malonate	66	1,2-Dimethylnaphthalene
32	Methyl benzoate	67	1,8-Dimethylnaphthalene
33	*n*-Pentadecane	68	4-Chloroaniline
34	(+)-Pulegone	69	3-Chloroaniline
35	Ethyl benzoate	70	2-Aminoacetophenone

* Samples were obtained from Dr. G. Schomburg, MPI für Kohlenforschung, D-4330 Mülheim/Ruhr, G.F.R.

ponents (*e.g.*, 13, 14 and 16). This increased selectivity for molecules with functional groups can be of distinct advantage in certain applications, *e.g.*, when hydrocarbon background or hydrocarbon component suppression is desirable, as may be the case in specific probing with this reactant for acidic protons by hydrogen–deuterium exchange[12]. With CH_3O^2H (or CH_3OH), ionization became so selective that less than half of the 70 components remained, for practical purposes, sufficiently detectable. The attempts to recognize and identify components only on the basis of unchanged retention times in other runs were ambiguous, if not futile, without careful reference to the three parallel FID traces. This may be illustrated by components 48–54, which

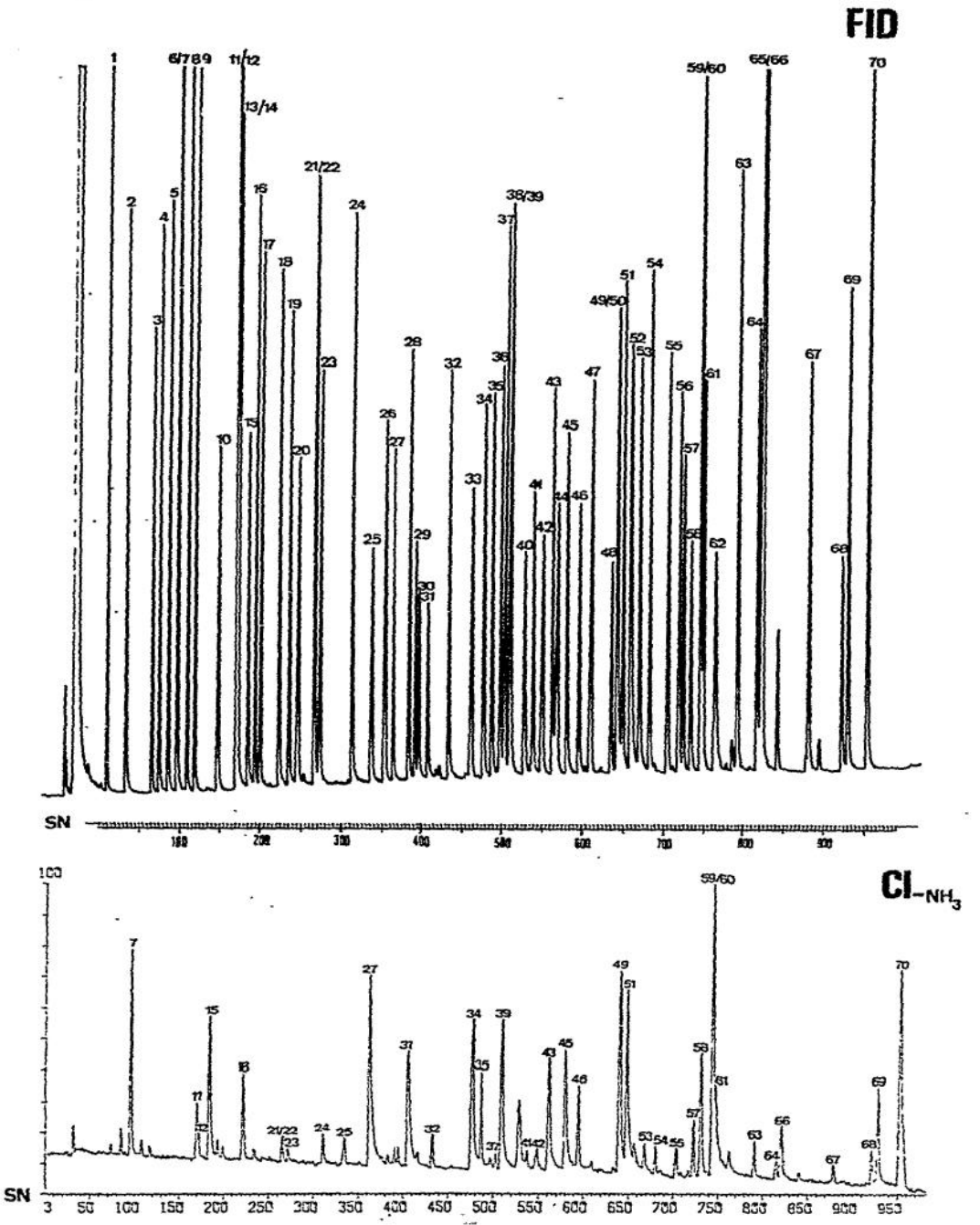

Fig. 5. Comparison of computer-reconstructed total-ion-current (lower trace, NH_3 reactant) and flame-ionization detection (upper trace) for a synthetic mixture (*cf.* Table I). Column as in Fig. 1. Mass range of digital TIC integration, *m/e* 72–350.

represent a tightly adjacent group exhibiting large discrepancies in the CI responses to CH_4 compared with those to isobutane and CH_3O^2H. In such a case it is necessary to identify the components by means of their spectra rather than their retention behaviour, particularly when overlapping of the components is complete (*e.g.*, 49 and 50). With the exception of isomers, this will also permit to detect which of the overlapping components are lost if they fail to respond when a new reagent gas is employed (*e.g.*, 6, 13 and 14, when substituting methanol for isobutane). In reality, the concentrations of the components are likely to differ over much larger ranges than in the present test mixture, and this may constitute another source of ambiguity in correlation work of this type.

The near-synchronous analog recording of the FID signal and the electronically integrated TIC (time lag *ca.* 1 sec with this configuration) yields traces having essentially superimposable time scales, which permit a careful timing of representative mass scans and their exact localization in the complex patterns of the chromatograms without tedious interpolation. However, in most cases, spectra will be recorded continuously in large numbers during the CI experiments rather than in single scans, and will be processed by means of a data system (*cf.* the Experimental section). This technique is illustrated by the TIC–RGC plot of the CI(NH_3) run of the same mixture (Fig. 5, lower curve). Although the TIC–RGC records differ considerably from analog FID records in their format, the calibration of both traces in identical spectrum numbers (SN) secures a quick and straightforward reference between the unlike traces. Correlations of data from different runs, by comparison of indexed spectra, thus become a matter of quick extraction of the spectra from corresponding sets or files. In spite of some loss in the apparent GC resolution of the TIC–RGC trace, owing to the pronounced incremental nature of the TIC sampling in this mode (only one sample per complete scan cycle; *i.e.*, 2 sec), this type of search for the most representative and exactly analogous spectra is preferred for practical work.

The great wealth of complementary data of independent, yet interrelatable, GC–CIMS experiments can be safely and reasonably managed only in this manner for more than a very few components of a mixture of some complexity. Only in this fashion can this wealth be exploited in an approach that aims to determine the structural features, one by one, for many compounds, rather than many features for one compound at a time.

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