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GAS CHROMATOGRAPHIC DETERMINATION OF ORGANIC IMPURITIES IN SOLVENTS FOR LIQUID CHROMATOGRAPHY

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SUMMARY

Methods for the gas chromatographic determination of organic impurities (with a detection limit of $5 \cdot 10^{-4}$–$5 \cdot 10^{-5}$%) in solvents for liquid chromatography have been developed to supply technologists with a reliable means of analytical control control in the commercial production of high-purity solvents. The series of solvents investigated included acetonitrile, methanol, ethanol, methylene chloride, formic acid, dimethylformamide, pyridine, tetrahydrofuran and dimethyl sulphoxide. Data on the content of major impurities in these above solvents and conditions for quantitative analysis are presented.

INTRODUCTION

High-performance liquid chromatography (HPLC), particularly the reversed-phase gradient elution variant, requires exceptionally pure solvents for use in the mobile phase. Accordingly, there is a need to produce chemicals of "highly pure for liquid chromatography" grade.

Impurities in the solvent can interfere in HPLC in three ways: (1) increasing the detector background noise; (2) causing severe baseline drift and "ghost" peaks; and (3) affecting retention data.

An increase in the background noise reduces the detector sensitivity and in some instances can mask the peaks of sample impurities. Numerous examples cited in the literature are concerned with UV detectors[1,2]. Thus, for instance, saturated hydrocarbons (say, *n*-hexane) provide the necessary light transmission up to 190 nm. However, olefinic impurities (1-hexene) present at a level of a few thousandths of 1% increase the minimum wavelength to 260 nm. According to our data, $5 \cdot 10^{-4}$% of acrylonitrile in acetonitrile reduces, at 200 nm, the transmission of the latter from 50 to 15%, and 0.001% of hydrazine reduces the pyridine transmission, at 320 nm, from 70 to 52%. Similar selective effects of impurities in the solvent on the background noise may also be expected for electrochemical and fluorescence detectors.

Ghost peaks and baseline drift caused by insufficient purity of the solvent are usually observed in gradient elution[3]. Under isocratic conditions, the chromatographic system (internal surfaces of sample injectors, connecting tubing, columns and

detector and sorbents in the guard or pre-column and separation column) in the frontal mode adsorbs and accumulates impurities from the solvent. Once equilibrium has been reached, the baseline becomes stabilized. However, as gradient elution proceeds the eluent composition varies and equilibrium is disturbed, giving rise to baseline drift and ghost peaks. To eliminate this undesirable effect without losing the high efficiency of the system, high-purity solvents should be employed for preparing mixed mobile phases.

HPLC with reversed-phase materials uses sorbents based on a silica gel support to which different radicals are grafted. The degree of surface coverage with radicals characterizes the quality of the material[4]. Generally, 100% coverage of the surface hydroxyl groups is impossible. For this reason, say, alkaline impurities may interact with the unprotected surface of the silica gel or be irreversibly adsorbed on it. Under such conditions the properties of the sorbent may vary, affecting the reproducibility of the retention data.

The purity of an eluent can be readily evaluated with a scan spectrophotometer by measuring ultraviolet light absorption in the range 190–350 nm. Unfortunately, this procedure cannot be considered exhaustive as far as the technology of solvent purification is concerned. The search for purification methods and their development includes the detection and identification of "limiting" impurities, the development of a quantitative assay for individual components and control in every purification step. Necessary information cannot be provided only by spectrophotometry; it is a combination of the latter with gas chromatography and gas chromatography–mass spectrometry that supplies reliable methods of analytical control.

The experience gained in the production technology of high-purity solvents[5] for various applications has made it possible to obtain a series of solvents (acetonitrile, methanol, ethanol, methylene chloride, formic acid, dimethylformamide, pyridine and tetrahydrofuran) suitable for HPLC. They contain 99.5–99.9% of the named substances, not more than 10^{-4} 10^{-3}% of unsaturated compounds and 10^{-2}–10^{-1}% of water. In this paper we consider the gas chromatographic analysis conditions for the above solvents and discuss the peculiarities of some of the techniques.

EXPERIMENTAL

Experiments were conducted on Tsvet-100 gas chromatographs with 1–3 m × 3 mm I.D. metal columns and 2 m × 3 mm I.D. glass spiral (60 mm loop diameter) columns fitted with dual flame ionization detectors. The columns were packed with sorbents by a microvibrator under vacuum conditions provided by a water-jet pump. The solid supports used were Dinochrom P (0.25–0.315 mm) (Reakhim, U.S.S.R.), Chromaton NAW (0.25–0.315 mm), Chromaton NAW DMCS (0.25–0.315 mm) (Lachema, Brno, Czechoslovakia) and Celite 545 (60–80 mesh) (LPC Chemical and Dyes, London, U.K.). For the analysis of formic acid, the columns were packed with the porous polymeric sorbent Polysorb-I (0.25–0.50 mm) (Reakhim), which is close in its properties to Porapak Q.

Helium was used as the carrier gas at a flow-rate of 30–60 ml/min. The flow-rates of hydrogen and air for feeding the detectors were 30 and 300 ml/min, respectively.

Samples were injected with an MSH-10 microsyringe into a metal evaporator, or directly into glass columns.

Chromatograms were evaluated using a C-1RB computing integrator (Shimadzu, Japan) with a standard program.

An internal standard method was used for quantitative analysis, the internal standard being added to samples in amounts of 0.5–1.0%. The detection limit of "limiting" impurities was $5 \cdot 10^{-5}$–10^{-4}%.

Peaks were identified by the addition technique with the use of retention parameters and data obtained on an LKB 2091 gas chromatograph–mass spectrometer (LKB, Uppsala, Sweden).

UV spectra were recorded with a Specord UV–VIS spectrophotometer (Carl Zeiss, Jena, G.D.R.).

RESULTS AND DISCUSSION

The chromatographic conditions for the solvents mentioned are summarized in Table I. The peculiarities of the analysis of some of them are discussed below.

Acetonitrile

The starting acetonitrile, being a by-product of acrylonitrile production by oxidative ammoniolysis, contains the following major impurities: acrylonitrile (up to 0.05%), propionitrile (10^{-3}%), allyl alcohol (0.5%), acetone (0.1%), *tert.*-butanol (0.05%), toluene (0.01%), methanol (0.005%), benzene (0.005%), methyl pentyl ether (0.005%), *o*-xylene (0.003%) and water (0.5%). The amounts of individual impurities in different batches of starting acetonitrile vary over a wide range (10–50 times). A three-step purification reduced the water content of acetonitrile by an order of magnitude, and the total organic trace content to 0.05%, thus providing a product with spectral characteristics meeting the requirements of HPLC. In the first step the starting material was treated with potassium permanganate, in the second step it was distilled, the final step being sorption of impurities by active alumina.

In choosing a sorbent to give the best resolution we tried a number of stationary phases usually recommended for the separation of polar compounds, including nitriles: β,β'-oxydipropionitrile, β-diethyldicyansulphide, Carbowax of molecular weight from 300 to 3000, 1,2,3-tris(β-cyanoethoxy)propane, tris(β-cyanoethyl)acetophenone, di(β-cyanoethoxy)hydroquinone and nitrilotripropionitrile. The first two appeared to be unsuitable for operation with a flame ionization detector because of their high volatility under the conditions used. Carbowaxes separated allyl alcohol from acetonitrile fairly well, but were inefficient with respect to other impurities. 1,2,3-Tris(β-cyanoethoxy)propane failed to separate allyl alcohol. The best results were obtained with 10% nitrilotripropionitrile on Celite 545, with a column length of 3 m, a temperature of 90–95°C and *sec.*-butanol as the internal standard. A representative chromatogram of the starting acetonitrile is shown in Fig. 1.

Methanol

The dehydration and purification of aliphatic alcohols in general and of methanol in particular were achieved by treating them with an aluminium alkoxide (aluminium methylate in this particular instance) at the boiling point:

$$3H_2O + Al(OCH_3)_3 \rightarrow Al(OH)_3 + 3CH_3OH \quad (1)$$

TABLE I

CHARACTERISTICS OF HIGH-PURITY SOLVENTS FOR LIQUID CHROMATOGRAPHY AND GAS CHROMATOGRAPHIC ANALYSIS CONDITIONS

Solvent	*Physical properties**				*Product composition***		*Analysis conditions****			
	η (cP)	*B.p. (°C)*	*RI*	*λ (nm)*	*Major impurities*	*C (%)*	*t_c (°C)*	*l_c (m)*	*Sorbent*	*Internal standard*
Acetonitrile	0.34	82	1.341	190	Acrylonitrile, allyl alcohol, acetone, *tert.*-butanol	99.9	95	3	10% nitrilo-tripropionitrile on Celite	*sec.*-Butanol
Methanol	0.54	65	1.326	205	Acetyldehyde, acetal, methyl ethyl ketone	99.8	65	3	10% Carbowax on Celite	*n*-Propanol
Methylene chloride	0.41	40	1.421	233	*cis*- and *trans*-dichloro-ethylene, allylchloride, chloroform	99.85	65	3	10% Carbowax 300 on Dino-chrom	Butyl acetate
Ethanol	1.08	78	1.359	210	Methanol, propanol, acetaldehyde, acetone, ethyl acetate	99.5	75	3	10% Carbowax on Celite	Benzene
Pyridine	0.88	115	1.507	300	Hydrazine, methylthio-phene, benzene, toluene	99.9	85	3	5% octadecyl-amine + 10% Carbowax 300 on Celite	Pseudocumene
Tetrahydro-furan	0.46	66	1.405	212	Silvan, acetone, isopropanol, furan	99.7	90	3	5% octadecylamine + 10% Carbowax 300 on Celite	*n*-Propanol
Dimethyl-formamide	0.80	153	1.428	268	Methanol, ethanol, dimethylamine, di-methylacetamide	99.9	125	3	20% Carbowax 20M + 2.5% KOH on Celite	Allyl alcohol
Formic acid	1.97	101	–	–	Acetic acid	99.9	150	2	Polysorb-I	Ethyl pro-pionate

* η = Viscosity at 25°C; b.p. = boiling point; RI = refractive index at 25°C; λ = approximate wavelength below which the solvent is opaque.
** C = Content of main substance in purified product.
*** t_c = Column temperature; l_c = column length.

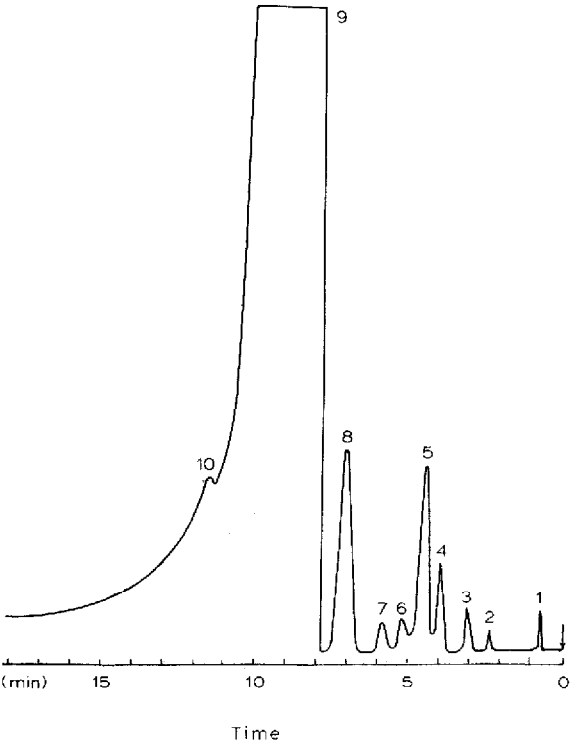


Fig. 1. Analysis of starting acetonitrile: 1 = diisopropyl ether; 2 = methanol; 3 = acetone; 4 = *sec.*-butanol (internal standard); 5 = toluene; 6 = unidentified impurity; 7 = acrylonitrile; 8 = allyl alcohol; 9 = acetonitrile; 10 = propionitrile.

The treated methanol was then distilled. The aluminium hydroxide formed as a result of aluminium methylate hydrolysis absorbs impurities, providing a complementary purification. In addition, aluminium alkoxides are capable of interacting with impurities such as acids, aldehydes, alcohols and ketones.

The starting methanol contained the following impurities: acetaldehyde (up to 0.05%), acetal (0.05%), methyl ethyl ketone (0.05%) and ethanol (0.01%). A quantitative analysis of samples was conducted on a 3-m column packed with 10% Carbowax 300 on Celite 545 with a column temperature of 65°C and *n*-propanol as the internal standard. The final product was UV-transparent methanol with a total content of organic impurities of about $5 \cdot 10^{-3}$%.

Methylene chloride

The starting methylene chloride contained the following impurities: 1,1-dichloroethylene (up to 0.02%), allyl chloride (0.005%), *trans*- and *cis*-1,2-dichloroethylene (up to 0.03 and 0.1%, respectively), chloroform (0.5%), 1,1,1-trichloroethane (0.01%), carbon tetrachloride (0.01%) and ethanol (0.05%). Ethanol should be present (0.08%) in the final product as a stabilizing admixture. The technology of methylene chloride purification included bromination of dichloroalkenes and removal of chloro- and bromoalkanes by distillation.

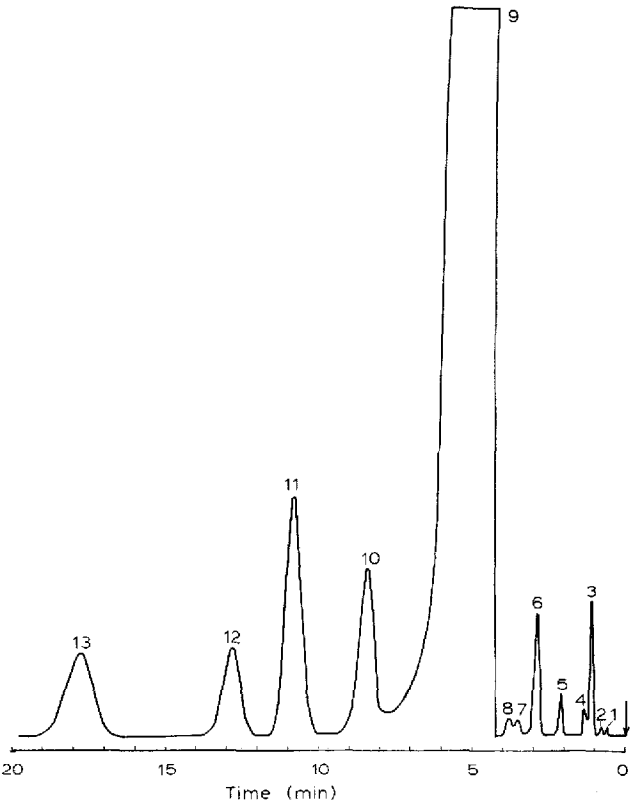


Fig. 2. Analysis of starting methylene chloride: 1, 2 and 4 = unidentified impurities; 3 = 1,1-dichloroethylene; 5 = allyl chloride; 6 = *trans*-1,2-dichloroethylene; 7 = carbon tetrachloride; 8 = 1,1,1-trichloroethane; 9 = methylene chloride; 10 = *cis*-1,2-dichloroethylene; 11 = chloroform; 12 = ethanol; 13 = butyl acetate (internal standard).

Quantitative analysis was carried out on a 3-m column packed with 10% Carbowax 300 on Dinochrom P (0.18–0.25 mm), the evaporator and column temperatures being 120 and 65°C, respectively, with butyl acetate as the internal standard (Fig. 2).

In calibrating the apparatus and conducting analyses, a weight correction factor had to be introduced because of the high volatility of methylene chloride, which increased the measurement error. Maintenance of this fraction factor at a constant level requires great skill of the operator. When an analysis is to be carried out under factory conditions, it is good practice to use internal normalization (with respect to correction factors), which needs no sample and standard weighing operations.

Formic acid

Raw formic acid was purified by vacuum evaporation (5–10 Torr) and further crystallization from the superheated vapour. The major impurity in formic acid is acetic acid. The flame ionization detector is selectively insensitive to formic acid, which is why tailing of the main component offered no difficulties in the determination of impurities eluting after it.

TABLE II

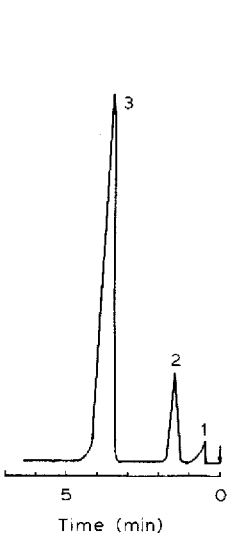
RETENTION TIME OF ACETIC ACID USING POLYSORB-I AND DIRECT SAMPLE INTERACTIONS

Concentration of acetic acid in formic acid (%)	*Relative retention time (with respect ethyl propionate), t_R (n = 11)*	*Relative standard deviation, S,*
0.02	0.405	0.007
0.3	0.406	0.004
0.4	0.403	0.005
7.0	0.364	0.003

The gas chromatographic analysis of free fatty acids is difficult[6]. For this reason, preliminary experiments were necessary to elucidate some problems concerning the sample injection into the column, the column material and the nature of the sorbent.

Direct sample injection into a glass column packed with the porous polymeric sorbent Polysorb-I gave good reproducibility of acetic acid retention times in the concentration range 0.02–7.0%, as shown in Table II.

As can be seen from the chromatogram in Fig. 3, the acetic acid peak is symmetric, indicating the absence of possible side-effects in the chromatographic system. This is also supported by the results below for the quantitative evaluation of chromatograms.



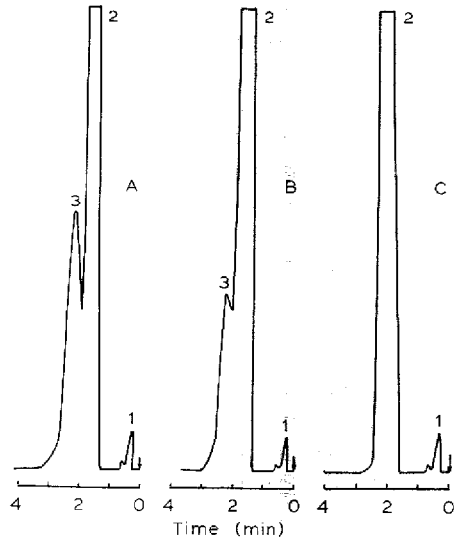


Fig. 3. Chromatogram of formic acid (1) with 0.15% of acetic acid (2) and 0.7% of internal standard (3) (ethyl propionate).

Fig. 4. Effect of sample injection zone temperature on appearance of a "ghost" peak on the chromatogram of a 10% acetic acid solution in water (2-m glass column packed with Polysorb-I, 150°C, sample volume 2 μl). 1 = Water; 2 = acetic acid; 3 = "ghost" peak. Sample injection zone temperature up to (A) 170°C, (B) 180°C and (C) 190–250°C.

Unfortunately, quantitative interpretation of the results was complicated owing to a dependence of the sensitivity coefficient, K_i, of the flame ionization detector (with respect to acetic acid) on the concentration C_i of the latter in solution. K_i was calculated from the known relationship $K_i = C_i S_{st}/C_{st} S_i$, where C_{st} is the internal standard concentration and S_{st} and S_i are the peak areas of the standard and acid, respectively. For the apparatus to be calibrated in the range of C_i from 0.01 to 10%, solutions of acetic acid and ethyl propionate in formic acid were prepared. As the raw formic acid contained up to 0.05% of acetic acid, samples with $C_i < 0.05\%$ could be prepared only by dilution with a solvent free from acetic acid. Water was used for this purpose because all the components of the mixture are water-soluble, and the position of the water peak on the chromatogram does not impede the evaluation of the impurity peaks of interest.

It was found that the injection of water-containing samples resulted in a peak on the trailing edge of the acetic acid peak. This peak corresponds to a relative retention time of 1.65 (with respect to acetic acid), its area being 5–12% of the acetic acid peak area. The peak width at the base increases for the observed mixed peak, when compared to pure acetic acid.

This "ghost" peak is absent from the chromatograms of single components of their water-free mixtures. It appears, however, on injecting an aqueous solution of acetic acid into the column.

The reasons for the "ghost" peak and main peak broadening were elucidated using the data obtained for a 10% acetic acid solution in water. Possible reasons may be as follows.

(1) Decomposition of acetic acid in the presence of water under the experimental conditions. This is hardly probable, as acetic acid in stable in both the liquid and vapour phases up to 250°C. Moreover, if we assume that decomposition does take place, the products formed should elute before rather than after the acid peak.

(2) The presence of water in the sample may lead to modification of the adsorbent surface. On the surface of Polysorb-I two types of adsorption sites may appear that differ in this energy of interaction with acetic acid molecules. The possibility of this double-site adsorption is also unlikely, first because the hydrophobic surface of Polysorb-I cannot retain water at 15°C. Second, successive injections of pure water and pure acid into the column should lead to surface modification as with the injection of their mixture. However, acetic acid injected soon after water is recorded as a single peak.

(3) Under normal conditions pure acetic acid occurs as associates. Hydrates of different composition are formed in its aqueous solutions. Under gas chromatographic conditions, associates must decompose because at the column outlet the acetic acid is recorded as a single peak. It may be assumed that under certain conditions a hydrate, stable in the vapour phase, is formed, which is separated in the column from the acid basic peak and is displayed as a single peak on the "tail" of the former. This new compound is formed not in the vessel with the initial sample solution but in the heated sample injection zone. This is evidenced by the chromatograms in Fig. 4, from which the "ghost" peak is seen to disappear when the temperature of the above zone is reduced to 170°C. Thus a method for the elimination of "ghost" peaks has been found. However, special investigations are required to elucidate the reasons for its appearance and the mechanism of the process.

TABLE III

EFFECT OF ACID CONCENTRATION AND SOLUTION COMPOSITION ON RELATIVE SENSITIVITY COEFFICIENT, K_i, OF FLAME IONIZATION DETECTOR WITH RESPECT TO ETHYLPROPIONATE

System	*Concentration of acetic acid (%, w/w)*							
	0.01		*0.1*		*1.0*		*10.0*	
	K_i	S_r*	K_i	S_r*	K_i	S_r*	K_i	S_r*
Formic acid–acetic acid	–	–	2.15	0.07	1.95	0.05	2.60	0.05
Dimethylformamide–acetic acid	1.47	0.09	2.04	0.03	2.14	0.09	2.67	0.02
Formic acid–water–acetic acid	–	–	1.94	0.07	"Ghost" peak on chromatograms			
Average	1.47		2.04		2.04		2.64	

* S_r = standard deviation; $n = 5$; confidence level $P = 0.95$.

Dimethylformamide was also tried as the diluent. As follows from the data listed in Table III, the value of K_i is independent of the composition of the medium but is determined by the acetic acid concentration. Using dimethylformamide as the diluent, samples containing $5 \cdot 10^{-5}$% of acetic acid were prepared. With a sample of 10 μl the acetic acid peak area was 30.6 mm^2 (height 10 mm, width 1.7 mm). The detection limit of acetic acid was calculated to be about 10 ng.

As can be judged from the data in Table IV, the analytical technique developed

TABLE IV

EFFECT OF CONCENTRATION OF ACETIC ACID ON ACCURACY OF ITS QUANTITATIVE DETERMINATION

Acetic acid concentration, C (%, w/w)		*System*			
		Formic acid–acetic acid		*Dimethylformamide–acetic acid*	
		C (%, w/w)	S_r*	*C (%, w/w)*	S_r*
0.01	injected	–	–	0.0090	–
	found	–	–	0.01	0.001
0.1	injected	0.16	–	0.087	–
	found	0.157	0.004	0.09	0.002
1.0	injected	0.93	–	0.997	–
	found	0.99	0.02	0.98	0.05
10.0	injected	9.35	–	9.77	–
	found	9.52	0.17	9.56	0.09

* S_r standard deviation; $n = 7$, $P = 0.95$.

provides good reproducibility and accuracy of quantitative results for acetic acid in the concentration range 0.01–10%.

Hence gas chromatography may be a successful substitute for the standard chemical method for the determination of acetic acid in formic acid, which consists in the decomposition of the latter by yellow mercury oxide at 110–140°C in an aqueous solution, filtration, washing the filter cake with water and titrimetric determination of acetic acid in the filtrate. The duration of this chemical analysis is about 2 h. If the concentration of acetic acid is less than 0.1%, the reliability and reproducibility of the results are unsatisfactory, and the chemical analysis method is unsuitable for application in the technology of producing high-purity formic acid for liquid chromatography, and in certifying the final product.

CONCLUSION

The statics and kinetics of solvent purification by chemicals, distillation, adsorption and crystallization have been investigated using gas chromatography. This allowed the substantiation of optimum production technology to give products that satisfy the requirements of HPLC. Gas chromatographic analysis has been introduced and successfully employed as the major analytical control method for finished products at factories producing solvents for liquid chromatography.

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REFERENCES

1 L. R. Snyder and J. J. Kirkland, *Introduction to Modern Liquid Chromatography*, Interscience, New York, 2nd ed., 1979, p. 252.
2 P. R. Brown, *High Pressure Liquid Chromatography*, Academic Press, New York, 1973, pp. 30–36.
3 S. M. McCown, B. E. Morrison and D. L. Southern, *Int. Lab.*, June (1984) 76–82.
4 N. H.C. Cooke and K. Olsen, *J. Chromatogr. Sci.*, 18 (1980) 512–524.
5 G. A. Egorenko, G. Z. Blyum, N. I. Samsonova, A. S. Lavrenova, V. A. Falin and Yu. M. Fetisov, *Chem. Ind.*, 112 (1978) 918–920.
6 K. I. Sakodynsky, G. A. Smolyaninov, V. Yu. Zelvensky and N. A. Glotova, *J. Chromatogr.*, 172 (1979) 93–105.