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The Development of Circulation Gas Chromatography

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The present state of circulation gas chromatography, and its principal regular features and apparatus, have been examined. A highly effective version of circulation gas chromatography has been proposed. It has been shown possible to achieve a high efficiency in the separation of organic compounds with similar structures and properties (several tens of thousands of theoretical plates with a specimen of up to 1 g).
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I. INTRODUCTION

In recent years, as a result of the intensified study in the field of present-day organic chemistry, it has become necessary to carry out the fine preparative separation of organic compounds showing extremely small differences in their structures and properties (for example, similar structural and spatial isomers). Attempts to solve this problem using the classical methods encountered in laboratory practice (distillation, extraction, crystallisation, etc.) do not always give the desired results. Moreover, the restricted nature of the possibilities provided by these methods becomes increasingly apparent with the increased complexity of the task of fine preparative separation. The difficulty of separating isomers is also increased by the fact that newly synthesised organic compounds are often available only in very small quantities. At the same time, the extremely marked differences in the chemical properties and biological activities of a number of isomeric molecules make the problem of their separation and individual study extremely important.

The present-day level of gas-chromatographic procedures and techniques makes it possible to separate substances with extremely similar structures and properties. In most cases, however, chromatographic methods, which have a high efficiency of separation, have an extremely low productivity, making it possible to work only with specimens with masses of 10^{-3}–10^{-6} g. These systems — capillary columns, very long (up to 100 m) packed columns with a small diameter, and short packed columns included in a circulation scheme — are used successfully to separate multicomponent mixtures, similar structural and spatial isomers, and isotopes and isotopically substituted compounds. The efficiency of the preparative separation of specimens of a mixture of substances, however, even in amounts corresponding to several tenths of a gram, is usually much lower, and rarely exceeds 3–5 thousand theoretical plates (t.p.). At the present time, in gas chromatography, the only methodological version making it possible to separate gram quantities of substances with an efficiency of about 30–50 thousand t.p. is apparently preparative circulation chromatography.

Since the publication of the first reviews of circulation gas[1] and liquid[2] chromatography, new papers have been published, developing the theory and extending the range of application of this method.

The present review examines chiefly development circulation gas chromatography (CGC), which is not, however, the only method of circulation separation. Versions of the circulation method have found application in heat-dynamic gas,[3] liquid,[4-29] and thin-layer[30] forms of chromatography. The preparative separation of a number of substances has been described.[31-34] Capillary circulation chromatography appears promising for some cases of extremely fine separation.[35,36]

II. VERSIONS OF THE CIRCULATION METHOD AND APPARATUS

The idea of circulating the specimen to be separated in a closed cycle with a layer of sorbent, suggested by Martin,[37,38] found practical application in two different types of technical apparatus. In the first case, the circulation of the specimen and the mobile phase is carried out in a single cycle by the action of a circulating pump. In the second version, recirculation of the mobile phase does not take place, and the circulation of the band of compounds being separated is brought about by a periodic change in the direction of the gas stream by means of special tap or valve switching devices.

In 1959–1960, Porter and Johnson[39-41] described the first circulation apparatus consisting of a closed circuit with two chromatographic columns, detector, input device, and peristaltic circulation pump. A similar apparatus, differing only in the replacement of the peristaltic pump by a piston pump, was later used.[42,43] With apparatus of this type, considerable broadening of the chromatographic peaks was observed, because of the mixing action of the pump and the large dead volumes in the closed system, and this made it impossible to obtain a high efficiency of separation. Moreover, the temperature range of operation of these circulation pumps was found to be extremely restricted.

In the period 1960–1970, circulation apparatus with a periodic action and switching devices appeared,[44-50] in which the band of chromatographic compounds circulated without passing through the pump. This made it possible to increase the efficiency of the separation. The turning of the taps, however, leads to marked pneumatic disturbance, associated with the redistribution of the pressures in the column. This leads to additional broadening of the chromatographic band, and a large number of cycles cannot be carried out. In a

comparison of the two systems described, preference was given[49] to the circulation scheme with a pump in the main cycle.

Circulation chromatography developed considerably by the use of gas stream switching devices in various circulation schemes with a semi-continuous or continuous action, designed mainly for preparative and industrial chromatography. Among the semi-continuous systems, mention may be made of an apparatus in which portions of the mixture to be separated are introduced in each half-cycle into the middle section of the circulation band, and the separated products are removed by cutting off the end sections of the chromatographic zones of each component.[51,52] Systems with a continuous action include circulation apparatus in which the specimen is introduced by the alternate opening and closing of taps arranged round the circumference of a toroidal column, with stationary columns,[53-55] and apparatus in which the supply section remains stationary as a result of the rotation or reciprocating movement of the columns.[56-62] These versions of toroidal circulating assemblies can also operate under periodic conditions.[63,64] Circulation assemblies based on the use of frontal chromatography have also been developed.[65-67] Although they have a high productivity, these assemblies have not solved the problem of the highly effective preparative separation of similar structural and spatial isomers or isotopically substituted compounds, which represents the most difficult problem for the organic chemist and technical engineer.

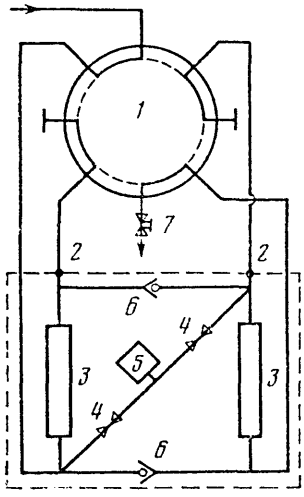


Figure 1. Circulation apparatus with unheated switching device: *1*) circulation tap, *2*) input devices, *3*) chromatographic columns, *4*) pneumatic resistance, *5*) detector, *6*) stream chopper valves, *7*) valve.

An unsatisfactory feature of many circulation schemes with gas stream switching devices is that the mixture being separated passes through the channels of the switching taps or valves. This makes it necessary to heat the switching assemblies, and this decreases their reliability of operation and the temperature range of application of the method, increases the dead gas volumes, and prevents the elimination of possible degradation of heat-sensitive compounds when they come into contact with the heated metal surfaces. In these schemes it is difficult to use pieces of apparatus made of glass.

To overcome these disadvantages, circulation schemes in which the switching tap is brought out of the thermostat have been proposed. In this case, the temperature restrictions are determined only by the thermal stability of the stationary liquid phase. The removal of the switching tap from the circulation circuit, however, led to considerable non-productive losses of the carrier gas and the substances being separated; these were lost to the atmosphere through the chokes connecting the column inlets and outlets,[68-70] or through auxiliary columns with a high resistance to the gas stream.[71,72] Further progress in CGC was achieved by using check valves or gate valves with a forced action to divide the gas stream,[73-75] replacing the economically unsuitable chokes. One possible form of circulation scheme with removal of the switching tap from the heated zone is shown in Fig.1.

The development of the circulation method of separation has been reflected in a number of Soviet (LKhP-4, LKhP-71, LKhM-9) and imported instruments. The universal attachments, developed by the Special Design Office of the Institute of Organic Chemistry of the Academy of Sciences of the USSR, with manual control or with programming and automatic switching of the circulation tap, PTsU-1 and PTsU-2, and attachments for chromatography in water vapour and for switching columns, P-1 and P-2, have made it possible readily to combine various versions of a circulation scheme with analytical and preparative gas chromatographs, for example LKhM-8MD, LKhP-51, etc. A specialised capillary circulation gas chromatograph, Biokhrom-27, is being developed at present (Special Design Office, Institute of Organic Chemistry of the Academy of Sciences of the USSR).

III. PRINCIPAL THEORETICAL REGULAR FEATURES OF CIRCULATION GAS CHROMATOGRAPHY

1. Dependence of the Efficiency of Separation on the Number of Chromatographic Cycles Carried Out

Early theoretical studies of the dependence of the efficiency of separation on the number of cycles carried out in the circulation scheme assumed a linear increase in the number of theoretical plates with increase in the number of columns through which the specimen passed.[47,76,77] Experiments showed, however, that the rate of increase in the efficiency of the separation usually decreases with increase in the number of columns passed through. A similar decrease in efficiency was noted in Ref.49. Sakodynskii and co-workers[32,78,79] observed a considerable fall-off in the increase in efficiency with increased number of cycles in a circulation preparative assembly; to make fuller use of the possibilities provided by the circulation scheme, the end zones of the peaks were removed without waiting for their complete separation.

A similar fall-off in the rate of the increase in the efficiency of separation with each new cycle was demonstrated in Refs.80 and 81. The observed effect was attributed to the influence of non-stationary regions in the gas stream, produced when the circulation tap was turned. As a result of the sharp redistribution of pressure in the columns when the tap is turned, part of the specimen in the gas phase is rapidly compressed, and moves forward relative to that part of the specimen present in the sorbed state in the stationary phase; for a finite rate of mass transfer, this leads to additional broadening of the chromatographic band.

Under the conditions described above, it was found appropriate to use long columns (10 m or longer),[33] which make it possible to reduce the number of times the circulation tap is turned and hence to decrease the rate of broadening of the chromatographic bands of the compounds being separated throughout the entire length of the column. Similar considerations apparently led other workers[82-85] to use columns with a length of 8–15 m for the separation of isotopically substituted compounds.

The limitations in the efficiency of separation attainable using circulation chromatography, which appeared at this stage of its development, produced in some workers a certain scepticism,[86] which was overcome only after an extensive analysis of the effects of pulse contraction and broadening of the chromatographic zones.

2. Effect of Pulse Contraction of the Chromatographic Zone

The effect of pulse contraction[88-90] of the chromatographic zone received its name by analogy with the pulse thermal enrichment[87] of the chromatographic zone. The essential features of this effect are as follows. If in the first chromatographic column of the circulation scheme through which the carrier gas moves, the linear velocity of the mobile phase is greater than that in the second column (as a consequence of the presence of the stream divider), then in the first column the trailing edge of the zone after a time t passes through a distance

$$l_1 = tu_1/(1+k')$$

and the leading edge of the zone in the second column after the same time t passes through a distance

$$l_2 = tu_2/(1+k')$$

where u_1 and u_2 are the linear velocities of the carrier gas in the first and second columns, and k' the extraction coefficient. As a result of the removal of part of the carrier gas between the columns, $u_1 > u_2$, that is $l_1 > l_2$. Thus the transfer of the band from one column to the other is accompanied by a contraction of the chromatographic zone in the ratio

$$b = l_2/l_1 = u_2/u_1 = 1 - a/100$$

where a is the mass fraction of the carrier gas removed between columns 1 and 2, expressed as a percentage. Thus the turning of the circulation tap will lead to a contraction of the chromatographic zone.

For columns consisting of a large number of identical sections, the width of the peak ν_m, the distance between the maxima of the peaks Δn_m, and the degree of separation R_m alter with change in the number m of columns passed through, as follows:

$$\nu_m = \nu_1 (m)^{1/2} \quad (1)$$

$$\Delta n_m = \Delta n_1 \cdot m \quad (2)$$

$$R_m = R_1 (m)^{1/2} \quad (3)$$

where ν_1, Δn_1, and R_1 are the parameters of the chromatographic band after its passage through the first column. Eqns.(1)–(3) describe the linear increase in the efficiency of separation with increase in the number of columns passed through.

Under pulse conditions, the width of the zone at the start of the second column is $\nu_1^0 = b\nu_1$. As a result of the broadening of the zone on passage through the second column, the width will be

$$\nu_2 = (b^2+1)^{1/2}\nu_1$$

After the transfer of the zone to the third column, the width of the band is reduced to

$$\nu_2^0 = (b^4+b^2)^{1/2}\nu_1$$

after which it increases to the following value:

$$\nu_3 = (b^4+b^2+1)^{1/2}\nu_1$$

As a result of the alternate contraction and broadening of the band, the width of the chromatographic zone after passage through m colums will be

$$\nu_m = [b^{2(m-1)} + b^{2(m-2)} + \ldots + b^2 + 1]^{1/2}\ \nu_1 = \left(\frac{1-b^{2m}}{1-b^2}\right)^{1/2}\nu_1 \quad (4)$$

Thus the broadening of the zone of a chromatographic compound in the circulation zone with removal of some of the gas between the columns is less than that given by Eqn.(1). The increase in the width of the zone is restricted to the limit

$$\nu_\infty = (1-b^2)^{-1/2}\nu_1$$

reached as $m \to \infty$.

Similar arguments can be used to examine the change in the distance between the maxima of the bands of two chromatographic compounds. After the zone has passed through m columns, the distance between the maxima of the bands will be:

$$\Delta n_m = \frac{1-b^m}{1-b}\cdot\Delta n_1 \quad (5)$$

From this equation it follows that in a circulation scheme with removal of gas, the increase in Δn_m is less than that expected from Eqn.(2). The value of Δn_m as $m \to \infty$ will be

$$\Delta n_\infty = \frac{1}{1-b}\cdot\Delta n_1$$

that is the distance between the band maxima in a circulation scheme with removal of gas is restricted to a certain limiting value.

Eqns.(4) and (5) give

$$R_m = \left(\frac{1+b}{1-b}\cdot\frac{1-b^m}{1+b^m}\right)^{1/2} R_1 \quad (6)$$

It follows from Eqn.(6) that the increase in the degree of separation is also restricted to the limiting value:

$$R_\infty = \left(\frac{1+b}{1-b}\right)^{1/2} R_1$$

The theoretical ideas about pulse chromatographic conditions were verified experimentally[89] using a model mixture of benzene and cyclohexane. The relationships obtained are given in Fig.2. When part of the gas stream is removed, the chromatographic zone eventually reaches an equilibrium state in which there is practically no further broadening of the zone, and simultaneously no further change in the values of ν_m, Δn_m, and R_m. The lack of agreement between the experimental curves and the curves corresponding to the theoretical equations (4), (5), and (6) is attributed to the effect of the pulse broadening of the zone.

3. Effect of Pulse Broadening of the Chromatographic Zone

The effect of pulse broadening of the chromatographic zone[90,91] is the opposite of the effect examined above, and is due to the existence of a gradient in the linear velocity of the carrier gas in the columns of the circulation scheme.

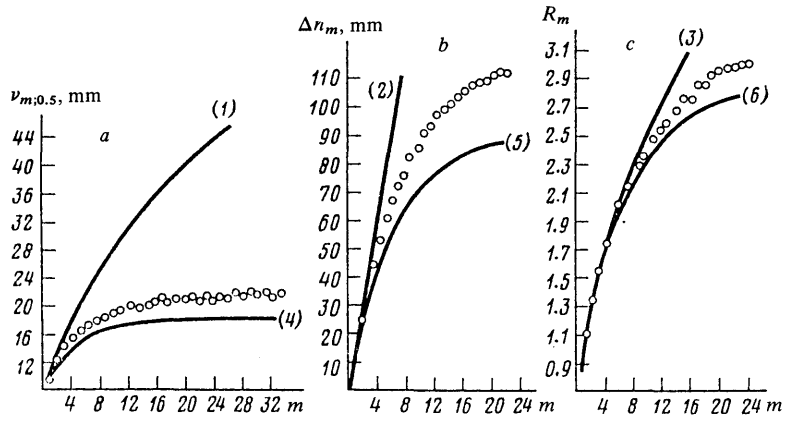


Figure 2. Dependence of the peak width at half-height $\nu_{m;0.5}$ (*a*), the distance between the maxima of the peaks Δn_m (*b*), and the degree of separation R_m (*c*) on the number of half-cycles m; the numbering of the curves corresponds to the numbering of the equations, and the points correspond to the experimental data. Conditions: two 4 m × 4 mm columns containing 5% Apiezon L, inlet pressures p_{in} = 1.1 MPa, outlet pressure p_{out} = 1.0 MPa, gas removal kept at a level of 12–13%.

The essential features of this effect are as follows. When there is no removal of gas between the columns, the linear velocity of the carrier gas in the columns increases continuously. The leading edge of the zone will move in the second column at an average velocity which is greater than that of the trailing edge remaining in the first column. The difference in the rates of movement of the edges of the zone, combined with the subsequent pulse redistribution of the velocities, will lead in each half-cycle to additional broadening of the bands of the chromatographic compounds, which increases from one cycle to another. Thus the movement of the chromatographic zone through the entire length of the column of the circulation scheme will take place slightly earlier than indicated by Eqns.(1) and (2).

The changes in the principal chromatographic characteristics with variation of the number m of columns passed through, with allowance for the effect of pulse broadening of the chromatographic zone, are given by the following equations:

$$b_0 = \bar{u}_2/\bar{u}_1$$

$$\nu_m = \left(\frac{b_0^{2m}-1}{b_0^2-1}\right)^{1/2} \nu_1 \qquad (7)$$

$$\Delta n_m = \frac{b_0^m - 1}{b_0 - 1} \cdot \Delta n_1 \qquad (8)$$

$$R_m = \left(\frac{b_0+1}{b_0-1} \cdot \frac{b_0^m-1}{b_0^m+1}\right)^{1/2} R_1 \qquad (9)$$

Here, b_0 is the zone broadening factor for the chromatographic compounds ($b_0 > 1$), and u_1 and u_2 the average linear velocities of the carrier gas in the first and second columns along the path of the gas.

According to Eqn.(9), the increase in R_m is restricted to the limiting value:

$$R_\infty = \left(\frac{b_0+1}{b_0-1}\right)^{1/2} R_1$$

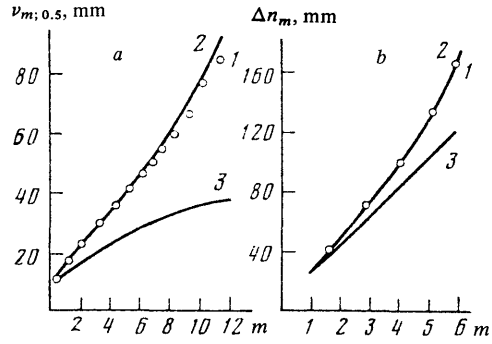


Figure 3. Dependence of the peak width at half-height $\nu_{m;0.5}$ (*a*) and the distance between the maxima of the peaks Δn_m (*b*) on the number of half-cycles m; *1*) experimental points; *2* and *3*) theoretical curves corresponding to Eqns. (7), (8) and (1), (2) respectively. Conditions: two 3 m × 4 mm columns containing 20% Apiezon L, p_{in} = 0.57 MPa, C = 1.24, no removal of gas.

The factor b_0 depends on the ratio C of the pressure at the inlet to the pressure at the outlet of the circulation assembly. For $C \leq 1.4$, it may be assumed that

$$\bar{u}_1 = (u_{out}/C + u_{1/2})/2$$
$$\bar{u}_2 = (u_{out} + u_{1/2})/2$$
$$u_{out}/u_{1/2} = [(C^2+1)/2]^{1/2}$$

where $u_{1/2}$ is the local linear velocity of the carrier gas at the outlet from the first column in the path of the gas. Thus b_0 is given by the expression

$$b_0 = \frac{[(C^2+1)/2]^{1/2}+1}{[(C^2+1)/2]^{1/2} \cdot \frac{1}{C}+1} \approx C^{1/2}$$

It follows from this equation that a decrease in C (for a constant pressure drop) leads to a decrease in the influence of the pulse effect in broadening the chromatographic zone. This conclusion has been confirmed experimentally.[92–95]

The dynamics of the change in the chromatographic parameters were studied using a circulation assembly with an eight-way tap in a scheme with two columns. The materials studied were the same as in the first case. Fig.3 shows that the above theoretical ideas about the pulse effect in broadening the chromatographic zone are confirmed qualitatively and quantitatively by the experiments. Only six half-cycles could be carried out without cutting off components.

Fig.4 gives the experimental dependence of the number of theoretical plates n on the number of half-cycles m under conditions of different ratios of the inlet and outlet pressures with no removal of gas between the columns (curves *1* and *2*).

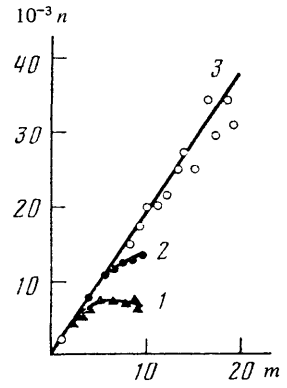


Figure 4. Dependence of the number of theoretical plates n on the number of half-cycles m: *1*) curve obtained at $C = 1.24$ (without gas removal) under the conditions described in Fig.2; *2*) curve obtained at $C = 1.06$ (without gas removal) under the following conditions: $p_{in} = 0.99$ MPa; *3*) straight line obtained under non-pulse chromatographic conditions for $C = 1.24$ ($a = 9.1\%$) at $p_{in} = 0.57$ MPa.

4. Non-pulse Circulation Gas Chromatography

The effect of pulse broadening of the chromatographic zone can be eliminated completely by compensating it by the effect of pulse contraction. This gives the optimum conditions of "non-pulse chromatography".†[90,91,96]

The optimum value, required to create these conditions, of the gas removal factor between the columns of the circulation scheme a can be estimated approximately from the material balance equation

$$S_1 u_1 d_1 = S_2 (u_2 d_2 + a u_1 d_1)$$

where S_1 and S_2 are the areas of the cross-section of the columns, occupied by the gas in the first and second columns of the circulation system, and d_1 and d_2 the densities of the gas in the chosen sections. When the sections of the columns are equal at points situated in the middle of the length of the columns, the following relationship will be observed:

$$a = 1 - u_2 d_2 / u_1 d_1$$

For non-pulse chromatographic conditions, $u_1 = u_2$, so that

$$a_{opt} = 1 - d_2/d_1 = 1 - p_2/p_1$$

since the density of the gas is proportional to the pressures p_1 and p_2 in the middle sections of the first and second columns.

For small values of a and C, the pressure in the columns decreases from p_{in} to p_{out} by an almost linear law. Under these conditions, taking the total length of the two columns of the circulation scheme as equal to unity, it is possible to write approximately:

$$p_1 = p_{in} - (p_{in} - p_{out})/4 = (3C/4 + 1/4)\, p_{out}$$
$$p_2 = p_{in} - 3(p_{in} - p_{out})/4 = (C/4 + 3/4)\, p_{out}$$

This gives

$$a_{opt} = 2(C - 1)/(3C + 1) \qquad (10)$$

Thus increase in the pressures at the inlet and outlet of the circulation scheme for a given pressure drop makes it possible to achieve values of C close to unity, leading to a corresponding decrease in the factor b_0. Complete elimination of the effect of pulse broadening of the chromatographic zone is achieved, however, by the pulse contraction of the zone, taking place when part of the gas stream is removed after the first column of the circulation scheme.

These ideas were verified[91] using a circulation scheme with controlled gas removal. The dependence of n on m, recorded under these conditions, was linear (straight line in Fig.4) over a fairly wide range of values of m (up to 19 half-cycles).

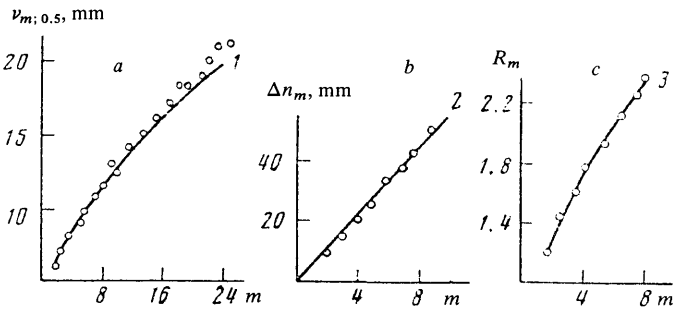


Figure 5. Dependence of the peak width at half-height $\nu_{m;0.5}$ (a), the distance between the maxima of the peaks Δn_m (b), and the degree of separation R_m (c) on the number of half-cycles m: *1*, *2*, *3*) theoretical curves corresponding to Eqns.(1), (2), and (3); the experimental points are marked with circles. Conditions: the column parameters are the same as those in Fig.2; $p_{in} = 0.82$ MPa, $C = 1.29$, $b_0 = 1.01$ for $a_{opt} = 12\%$.

Fig.5 gives the dependence of ν_m, Δn_m, and R_m on m, obtained for $b_0 = 1.01$ and $a_{opt} = 12\%$. The experimental points were found to be close to the theoretical curves *1* and *3* for ν_m and R_m, constructed using Eqns.(1) and (3), and to the theoretical curve *2* for Δn_m, constructed from Eqn.(2).

†The term "non-pulse chromatography" is possibly not entirely appropriate, since when the carrier gas moves from one column to another, its velocity undergoes an abrupt change at the moment when the tap is turned, that is the pulses are preserved. The term "non-pulse chromatography" reflects the fact that the pulse effects, which altered the principal regular features characteristic of the chromatographic process with circulation, disappear.

A decrease in the value of a_{opt} is extremely important in preparative chromatography. According to Eqn.(10), for $C = 1.06$ the value of a_{opt} would be reduced to 3%. On preparative columns[97] with dimensions 3 × 10 mm containing 20% Apiezon L at $p_{in} = 0.63$ MPa and $C = 1.068$ ($a_{opt} = 2.81 \pm 0.15\%$), a linear relationship was obtained between the number of theoretical plates n (with respect to hexane) and the number of columns m through which the chromatographic zone passed. Under these conditions, the preparative circulation apparatus can be regarded as a system of m columns with identical parameters, connected in series.

The losses ϕ of substance during circulation with removal of part of the gas stream between the columns are given by:[90]

$$\varphi, \% = [1 - (1 - a_{opt}/100)^{m-1}] \cdot 100 \qquad (11)$$

These losses can be eliminated almost completely either by the removal and repeated separation of the material removed, or by using hydrogen or a mixture of nitrogen and hydrogen as carrier gas, combined with a palladium separator.[98,99] The contraction of the chromatographic zone brought about by the pneumatic pulses arising when the circulation tap is turned can to some extent replace the use of thermal pulses.[100,101]

Table 1. Comparison of the parameters of the fine separation of benzene and hexadeuteriobenzene at $k' = 2$ in a long packed column (pc), the columns of a circulation assembly (pcc), and a capillary column with a thick layer of sorbent on the walls (c).

Parameter	Nitrogen			Helium		
	pc	pcc	c	pc	pcc	c
Diffusion coefficient in the gas phase at atmospheric pressure $10D_{g,0}$, $cm^2 s^{-1}$	1.06	1.06	1.06	4.14	4.14	4.14
Viscosity of the gas $10^{10}\eta$, kg s cm^{-2}	2.19	2.19	2.19	2.40	2.40	2.40
Diameter of carrier particles d_p, cm	0.02	0.02	0.02	0.02	0.02	0.02
Diffusion coefficient in the gas phase $10^2 D_g$, $cm^2 s^{-1}$	1.40	2.60	2.10	2.70	5.13	4.20
Permeability coefficient $10^7 K^0$, cm^2	3.95	14.04	16.20	3.95	14.58	16.20
Height equivalent to a theoretical plate HETP, cm	0.118	0.118	0.118	0.118	0.118	0.118
Column length l, cm	10620	425	10620	10620	425	10620
Mean linear velocity of the carrier gas $\bar{u}$, cm s^{-1}	1.40	2.60	3.55	2.70	5.13	7.08
Number of theoretical plates n	90000	3600	90000	90000	3600	90000
Number of half-cycles m	—	25	—	—	25	—
Separation time t_R, h	6.33	3.41	2.42	3.28	1.72	1.25
Duration of a half-cycle Δt, min	—	8.19	—	—	4.13	—
Inlet pressure p_{in}, MPa	1.12	0.47	0.70	2.34	0 97	1.49
Guiochon factor j_{pc}	0.81	1.00	0.84	0.78	1.00	0.80
HETP/$\bar{u}$, s^{-1}	0.084	0.045	0.032	0.043	0.023	0.016
$t_R/(t_R)_c$	2.62	1.41	1.00	2.62	1.38	1.00

Notes: separation factor of the components of the mixture 1.02, separation temperature 338 K, capillary column diameter 0.025 cm, fraction of the cross-section occupied by the gas in the capillary column $\kappa = 0.4$, attainable degree of separation $R = 1$.

Thus the ideas developed above about the effects of the pulse contraction and broadening of chromatographic zones, confirmed experimentally, can be used to estimate the place and importance of CGC relative to other chromatographic methods with similar efficiencies.

5. Comparison of the Parameters of Fine Separation in the Filled Columns of a Circulation Scheme and in Columns of Equivalent Length

Comparison of the parameters of fine separation (separation factor $\alpha - 1 \ll 1$) in circulation chromatography and in long packed columns[102-106] showed[107-109] that for a given degree of separation, the time taken for the analysis of a binary mixture is smaller by a factor of approximately 2–3 in the first case. This advantage of circulation chromatography increases as α approaches unity. Compared with long packed columns, circulation chromatography requires a pressure at the inlet to the column which is smaller by a factor of 3.5–4, and the length of the column can be reduced by a factor of 25–30.

Table 1[109] compares various parameters of fine separation in long packed columns, columns of a circulation assembly, and a capillary column with a thick layer of sorbent on the walls.[110,111] The rates of separation for the last two systems are similar. This is due to the relatively high permeability of a hypothetical column with separating power and analysis time equivalent to those of the columns of the circulation system. The slight increase in the HETP in the range of high velocities, observed in circulation chromatography, is much less than that in long columns. As a result of these factors, it is possible to achieve extremely high values of the efficiency of separation in capillary circulation chromatography on columns with a length of 7.5 m.[35,36]

Thus the method examined has extremely significant advantages over separation in long columns from the viewpoint of the total efficiency, separation time, magnitude of the pressure required, quantity of sorbent used, and necessary column length.

IV. THE EFFICIENCY OF THE COLUMNS IN PREPARATIVE CIRCULATION GAS CHROMATOGRAPHY AND METHODS FOR INCREASING THEIR PRODUCTIVITY

The expression for the HETP of a preparative column can be written as follows[112]

$$\text{HETP} = A^0 + \frac{2\gamma \cdot D_g}{\bar{u}} + \frac{8}{\pi^2}\left(\frac{k'}{1+k'}\right)^2 \frac{d_p^2}{D_g}\bar{u} + \frac{2k'}{3(1+k)^2}\frac{d_l}{D_l}\bar{u} + \frac{C_0 d^2}{4D_g}\bar{u}$$

where A^0 is the constant in the Van Deemter equation, γ the sinuosity coefficient, d_l the thickness of the liquid film, D_l and D_g the diffusion coefficients in the liquid and gas phases respectively, C_0 a constant, and d the column diameter.

For preparative columns containing 1–5% or less of the liquid phase,[113] by analogy with analytical columns, it is possible to write

$$\text{HETP} = \frac{2\gamma D_g}{\bar{u}} + \left\{\frac{\frac{C_0}{4}\left(\frac{d}{d_p}\right)^2 + \frac{C_0}{2}\left(\frac{d}{d_p}\right)^2 k' + \left[\frac{C_0}{4}\left(\frac{d}{d_p}\right)^2 + 0.81\right](k')^2}{(1+k')^2}\right\}\frac{d_p^2}{D_g}\bar{u} \qquad (12)$$

When the columns are carefully filled, the efficiences of preparative columns with relatively small diameters are comparable to those of analytical columns. If it is assumed that

$$\frac{C_0}{4}\left(\frac{d}{d_p}\right)^2 = 0.9$$

Eqn.(12) gives

$$\text{HETP} = \frac{2\gamma D_g}{\bar{u}} + \frac{0.9 + 1.8k' + 1.71(k')^2}{(1+k')^2} \cdot \frac{d_p^2}{D_g}\bar{u}$$

The form of the equation obtained is similar to that of the equation for analytical columns.[109]

It has been shown[114] that

$$\bar{u}_{pc} \approx 0.3\frac{\alpha-1}{d_p}[K^0(D_{r,0})_{pc}(p_{out})_{pc}/\eta]^{1/2}\{(k')^2/[0.9+1.8k'+1.71(k')^2]\}^{1/2} \quad (13)$$

where the subscript "pc" refers to the packed column. Substituting Eqn.(13) in the equation[115]

$$\Pi \approx 5\cdot 10^{-2}\left[\frac{d(\alpha-1)}{R}\right]^2 \varkappa c_g \bar{u}\frac{k'}{1+k'}$$

where Π is the productivity of the preparative chromagraphic assembly, and c_g the equilibrium concentration of the first and second components in the gas phase, gives

$$\Pi_{pc} \approx 1{,}5\cdot 10^{-2}\left[\frac{d(\alpha-1)}{R}\right]^2\frac{\alpha-1}{d_p}\varkappa c_g[K^0(D_{g\,0})_{pc}(p_{out})_{pc}/\eta]^{1/2}[\chi(k')]_{pc}$$

where

$$[\chi(k')]_{pc} = \{(k')^3/(1+k')^2[0.9+1.8k'+1.71(k')^2]\}^{1/2}$$

For the circulation system (subscript "pcc")

$$\Pi_{pcc} \approx 1{,}5\cdot 10^{-2}\left[\frac{d(\alpha-1)}{R}\right]^2\frac{\alpha-1}{d_p}\varkappa c_g\left[\frac{K^0_{pce}(D_{g\cdot 0})_{pc}(p_{out})_{pc}}{\eta}\right]^{1/2}[\chi(k')]_{pc}$$

where K^0_{pce} is the permeability coefficient of a hypothetical column equivalent to that used in the circulation system.

With allowance for the loss of substance during circulation (Eqn.(11)), the ratio of the productivities of the circulation system and the long packed column is given by

$$\left[\frac{\Pi_{pcc}}{\Pi_{pc}}\right] = \frac{1}{[C_{pcc}]^{(n-1)/2}}\frac{1}{2.12}\left[\frac{C_{pcc}-1}{C_{pcc}+1}\frac{1}{j_{pc}(\alpha-1)}\frac{1+k'}{k'}\right]^{1/2}$$

where j_{pc} is the Guiochon factor.[116]

These arguments show that for a given total efficiency and similar parameters of the columns used for the separation of substances with very similar properties ($\alpha = 1.02$), the productivity of long columns[117–119] is 2–2.5 times that of a circulation system. The productivity per unit volume of the sorbent,[47,120] however, is ~5 times greater for separation using circulation. This last feature is of considerable importance, since a decrease in the volume of sorbent is not only economical but also leads to a decrease in the volume of the apparatus and the expenditure of work and time in the preparation of the columns.

The efficiency and separating power of columns with length 2–4 m and diameter 10 mm in the preparative separation of mixtures with $1.02 < \alpha < 1.07$ by CGC have been studied.[121] Under conditions in which the removal of gas between the columns was negligibly small (~0.1% of the main stream), increase in the pressure at the outlet from the columns leads to an increase in the overall efficiency n and to an increase in the number of possible half-cycles m. At the same time there is an increase in the time taken for circulation, so that the productivity of the system for a constant volume of specimen added $M_0 = \text{const}$ decreases. Increase in M_0 leads to a decrease in the number of half-cycles and the number of theoretical plates.

Under the conditions of non-pulse circulation chromatography, the removal of gas leads to an additional decrease in productivity. In this case, however, there is a marked increase in the overall efficiency of the separation and an increase in the possible number of cycles. For large volumes of the added specimen and $C_{pcc} = 1.1$, the effect of the pulse broadening of the zone is of secondary importance, and a decisive contribution to the decrease in the overall efficiency is made by the influence of the volume of the specimen added.

The results show that it is appropriate to use CGC to separate compounds with very similar properties under non-pulse circulation conditions.

The decrease in the productivity of the circulation assembly compared with long columns can be avoided by the periodic introduction of the original mixture and removal of the separated components in semi-continuous circulation systems. This method has been used[4,122–124] to separate the alkali metals and various isotopes by ion-exchange chromatography.

For gas chromatography, a method for the semi-continuous separation of mixtures has been proposed,[51] in which, as the specimen is transferred from one column to another during circulation, a fresh portion of the mixture being separated is introduced each time into the supply section, situated between the maxima of the peaks of the components being separated. Subsequently, beginning from the moment when the total width of the zone becomes equal to the length of the chromatographic column, the ends of the chromatographic band are cut off, and the pure components are collected. The overall distribution curve of the component streams with periodic additional supply shows a clearly defined maximum, whose position coincides with the supply section (as a consequence of the superposition of a large number of Gaussian curves).

Circulation chromatography in which the enriched ends of the chromatographic band are cut off is characterised by a high purity of the products obtained. For the usual method of removing the separated zones of the chromatographic compounds, this quantity is given by the equation[125]

$$X_p = 1 - \frac{1}{2(2\pi R)^{1/2}}e^{-2R^2} \quad (14)$$

The value $R = 1$ from Eqn.(14) corresponds to the value $X_p \times 100 = 97.3\%$. The same quantity for circulation chromatography in which the enriched ends of the chromatographic band are cut off is given by the expression[97,126]

$$X'_p = e^{8R(R+1)}/(1+e^{8R(R+1)})$$

For $R' = 1$ the value obtained is $X'_p \times 100 = 99.99998\%$.

For $X_p = X'_p = 99.97\%$, the values obtained are $R \cong 2.8$ and $R' \cong 0.65$ using a column approximately ten times shorter in the circulation scheme.[97]

Thus a brief theoretical examination of the application of the circulation method with periodic additional supply, in which the ends of the chromatographic band are cut off, shows not only an increase in productivity but also the possibility of using this form of CGC to obtain substances with a high purity (≥99.97%).

V. SEPARATION OF ISOTOPICALLY SUBSTITUTED COMPOUNDS

In gas chromatography, the separation of isotopically substituted compounds is one of the most complex problems, requiring the use of highly efficient columns. Unfortunately, an increase in the separation factor by the use of selective liquid phases is almost impossible in this case, because of the extremely small magnitude of the isotope effects in the solution process.[127–129] In other words, change in the nature of the absorbent or liquid phase and the associated change in the adsorptive or solvent power cannot ensure success in the separation of compounds containing different isotopes of a given element.[130] Thus in the search for ways of solving this problem, the need to increase the efficiency of the chromatographic columns used is the most important feature to be considered.

In gas–liquid and gas–adsorption capillary chromatography, the efficiency of the columns can be increased by modifying the inner surface of the walls of the capillaries in different ways, or by depositing sorptive layers of different materials on the walls.[130]

Isotopically substituted compounds can be separated without using long capillary and packed columns of small diameter, by using short packed columns included in a circulation assembly. In the early stages of the development of circulation chromatography, fairly long columns were used. This made it possible to decrease the rate of broadening of the chromatographic band throughout the entire length of the column when the circulation tap was turned. The first isotopic separations[82] of methane, n-butane, cyclobutane, and their deuteriated and tritiated analogues were carried out on 15 m columns at atmospheric pressure at the outlet.

Columns with length 8 m, containing a solution of silver nitrate in ethylene glycol as stationary phase, have been used[83,84] for the gas-chromatographic separation of the isotopically substituted ethylenes C_2H_4, C_2H_3D, and $C_2H_2D_2$. The analysis using the circulation technique was more rapid than that using one long column; this is particularly important in the gas chromatography of isotopic molecules containing radioactive isotopes with short half-lives.

An attempt has been made[85] to separate the isotopes of carbon (^{12}C and ^{13}C) and sulphur (^{32}S and ^{34}S) as their volatile fluorides. The separation was carried out with Maxwell's circulation scheme[44] using two 8 m columns containing Porapak. Appreciable enrichment of the isolated fractions in the individual isotopes was achieved. Compounds labelled with radioactive isotopes (^{14}C, ^{35}S) were later analysed[131] on an automatic circulation gas radiochromatograph.

Table 2. Principal characteristics of the preparative gas-chromatographic separation of various isotopically substituted organic compounds by CGC on columns with dimensions 4 m × 23 mm.

Mixture being separated	Stationary phase	v, ml	w, %	L, m	α	$10^{-3}n$	HETP, mm	R
CH_3COCH_3—CD_3COCD_3	LAC-3R-728	0.90	39.9	108	1.012	35.5	3.0	0.56
C_6H_{12}—C_6D_{12}	LAC-3R-728	0.85	50.4	84	1.014	44.5	1.9	0.74
$C_6H_5CH_3$—$C_6D_5CD_3$	DC-550	0.50	44.0	84	1.013	44.0	1.9	0.68
C_6H_6—C_6D_6	DC-550	0.55	40.3	92	1.011	48.0	1.9	0.60
$C_6H_5C_2H_5$—$C_6D_5C_2H_5$	DC-550	0.50	28.7	128	1.006	74.5	1.7	0.41

Symbols: v is the volume of the specimen added, w the yield of separated products, and L the total column length traversed by the zones.

The separation of the carbon isotopes ^{12}C and ^{13}C as the oxide on molecular sieves, and the separation of the neon isotopes ^{20}Ne and ^{22}Ne, have been carried out;[132] appreciable enrichment in the isotopes was again achieved. Two columns with lengths of 0.5 m containing molecular sieves have been used[77] to separate the o- and p-isomers of H_2 and D_2. The separation factors were 1.032 for o- and p-hydrogen, 1.024 for protium deuteride and deuterium, and 1.019 for o- and p-deuterium.

The effects of pulse broadening and contraction of the chromatographic zones and the related increase in the efficiency of the process made it possible to separate benzene and hexadeuteriobenzene, and also benzene and trideuteriobenzene,[133] on columns with dimensions 4 m × 4 mm containing squalane as liquid stationary phase. In the last case, the compounds being separated passed through a total column length equivalent to 100 m, and the efficiency of the separation was ~120 thousand t.p. This high efficiency of separation was made possible by using non-pulse circulation chromatography conditions, characterised by a linear relationship between the number of theoretical plates and the number of columns passed through. The analytical separation of a number of oxygen-containing isotopically substituted organic compounds has been carried out:[69,134] C_2H_5OH–C_2D_5OD, CH_3COCH_3–CD_3COCD_3, iso-C_3H_7OH–iso-C_3D_7OD, under non-pulse CGC conditions.

The possibilities provided by preparative CGC for separating isotopically substituted organic compounds have been studied by the present authors.[135–137] The principal characteristics of the preparative gas-chromatographic separation of the mixtures studied by CGC are given in Table 2,[138] which shows that the efficiency of preparative separation by CGC reached several tens of thousands of t.p., which is 10–20 times the efficiency of long packed columns (dimensions 20 m × 9 mm),[113] and is comparable with the possibilities provided by capillary chromatography. Mass-spectrometric analysis showed that the purity of the fractions obtained was not lower than 95–97%. Fig.6 gives fragments of the chromatogram obtained in the preparative separation of toluene and perdeuteriotoluene.

As already noted, the productivity of circulation gas-chromatographic systems used to separate compounds with similar properties, requiring a highly efficient process, depends to a large extent on the quantity of eluate removed to maintain non-pulse chromatographic conditions. For the preparative separations listed in Table 2, this quantity was 2.0–2.4% of the total carrier-gas volume for a ratio of the

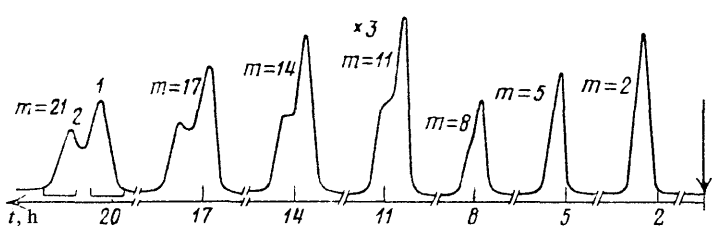


Figure 6. Fragments of the chromatogram for the preparative CGC separation of a mixture of octadeuteriotoluene (*1*) and toluene (*2*) on 4 m × 23 mm columns filled with DC-550 (15%). Conditions: temperature of the columns 105 °C, p_{in} = 0.64 MPa, C = 1.04, carrier-gas (nitrogen) velocity 400 ml min^{-1}, fraction of gas removed ~2%, initial loading 0.5 ml, yield of separated products 44%.

inlet and outlet pressures $C = 1.04-1.05$ and a pressure at the column inlet not exceeding 0.64 MPa. A decrease in the quantity C as a result of an increase in the inlet and outlet pressures (for the same given pressure drop) makes it possible to decrease the quantity of gas removed between the columns and hence to increase the productivity of the circulation assembly. Thus an increase in the pressure at the inlet into the system to, for example, 1.33 MPa (keeping the rate of supply of carrier gas at the outlet from the system unchanged) decreases the value of C to 1.023. This in turn makes it possible to decrease the quantity of gas removed between the columns and to decrease the loss during the separation of the above mixtures by 13–17%.

VI. SEPARATION OF ORGANIC COMPOUNDS WITH SIMILAR STRUCTURES AND PROPERTIES

A field in which circulation chromatography is irreplaceable is the fine preparative separation of the isomers of volatile organic compounds. In a number of cases, the similarity in the properties of these isomers is even closer than that for isotopic molecules. The difficulties of separating isomers are also increased by the fact that newly synthesised organic compounds are often available only in very small quantities, corresponding to fractions of a gram or milligrams.

The problem of determing the isomeric composition of newly synthesised organic compounds is now being solved using highly efficient capillary chromatography, but the problem of the preparative separation of isomers with similar properties still remains one of the most difficult unsolved problems in organic chemistry. At the same time, the high efficiency of separation characteristic of CGC makes it possible to solve the problem of both the analytical and the preparative separation of isomeric structures for the resolution of a wide range of problems encountered in present-day organic chemistry.

Thus the composition of the products of the intramolecular acylation of ω-(5-methylthienyl-2)-alkanoic acids with side chains of different length has been studied[139] by the chromatographic analysis of the isomeric macrocyclic ketones with a thiophene ring. The isomeric cyclic thienones were separated on 3 m × 4 mm columns with a sorbent containing 3% SE-30 at a temperature of 235 °C, a carrier-gas velocity of 55 ml min^{-1}, $p_{in} = 0.89$ MPa, and $C = 1.25$. Twelve half-cycles in 2 h gave the value $R = 1.04$ for $\alpha = 1.023$. The efficiency of separation amounted to ~64 thousand t.p. Good results have been obtained in the separation of the geometric isomers of high-boiling saturated aliphatic acids on columns containing 5% Apiezon L.[94] Methyl oleate and methyl elaidate were separated at 220 °C after 11 half-cycles at $p_{in} =$ 0.70 MPa and $p_{out} = 0.62$ MPa. The isomeric methyl linoleates were separated under similar conditions. The overall efficiency of separation in these experiments reached ~83 thousand t.p.

The *cis*- and *trans*-isomers of 1-ethyl-4-isopropylcyclohexane, 2-t-butyltetrahydrofuran, and 3-t-butylcyclopentanol have been separated on columns with length 3.5 m and diameter 10 mm, filled with the carrier Chezasorb with 5% XE-60.[70] An efficiency of separation of 3–8 thousand t.p. was achieved using a 20 mg specimen after 8–9 half-cycles. The same authors carried out the analytical separation of a mixture of the methyl esters of 1,3-dimethylcyclohex-3-ene-1-carboxylic and 1,4-dimethylcyclohex-3-ene-1-carboxylic acids — the isomeric products of a diene synthesis — with $\alpha = 1.044$. An efficiency of ~23.5 thousand t.p. with a separation factor of 1.04 was achieved after 8 half-cycles in 1.5 h.

A mixture of propylene oxide and propionaldehyde has been separated[140] by circulation gas chromatography on a column with Chromosorb W containing 30% dinonyl phthalate. The same author separated *m*- and *p*-xylenes after 3 half-cycles on two 45 cm columns filled with a sorbent containing 7.5% bentone-34 and 14.25% MS-555 silicone oil. The micropreparative separation of the isomeric tetramethylbenzenes

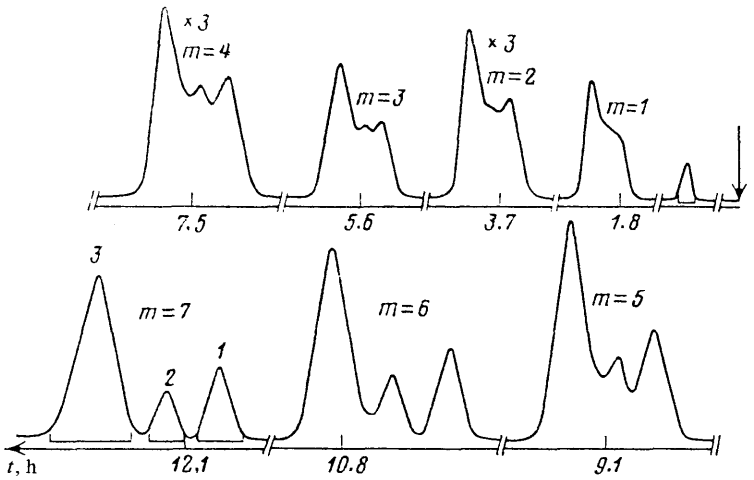


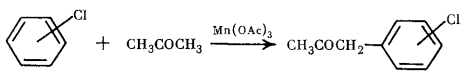
Figure 7. Fragments of the chromatogram of the preparative CGC separation of a mixture of *p*- (*1*), *m*- (*2*), and *o*-chlorobenzyl methyl ketones (*3*) on 4 m × 20 mm columns filled with LAC-3R-728 polyester (12%). Conditions: temperature of the columns 220 °C, $p_{in} = 0.58$ MPa, $p_{out} = 0.54$ MPa, carrier-gas (nitrogen) velocity 380 ml min^{-1}, removal of gas between columns 3.0%, original loading 0.5 ml, yield of separated products 83%.

durene and isodurene with an efficiency of separation of 26 thousand t.p. has been described.[115]

One of the advantages of CGC is its universal nature. As a result of the high efficiencies achieved by repeating the separation cycle, it is possible to obtain good results without using highly selective stationary liquid phases. Thus mixtures of the isomeric aromatic hydrocarbons: *m*- and *p*-xylenes, *p*-xylene and ethylbenzene,[137] and isomeric tetramethylbenzenes[115] were separated equally successfully by preparative methods on stationary phases which are not highly selective (LAC-3R-728, DC-550, and PEG-6000 respectively).

Circulation chromatography has also been used to study the kinetics of chemical reactions in reaction gas chromatography. Thus in a study of the kinetics of the Diels–Alder reaction between isoprene and maleic anhydride, the latter was deposited on Chromosorb P as stationary phase in the form of a solution in tricresyl phosphate. The change in the concentration of the volatile component isoprene was followed from the change in the area of the peaks recorded during circulation.[141]

To study the products of homolytic substitution in chlorobenzene by acetonyl radicals generated in the acetone–$Mn(OAc)_3$–AcOH redox system at 70 °C according to the published scheme,[142] the present authors[138] carried out the preparative separation of the mixtures of isomers formed, using highly efficient CGC.



The separation was carried out in an all-glass assembly with a gas-stream separating tap placed outside the thermostat.[75] Fragments of the chromatogram obtained are shown in Fig.7. Practically complete separation of all three isomers with an efficiency of separation of 12.5 thousand t.p. for the *p*-isomer was achieved after seven half-cycles, which corresponds to a total path length of the zones through the column of 28 m. The separation factors of the isomers according to the analytical chromatograms were 1.046 for *m*- and *p*-chlorobenzyl methyl ketones and 1.051 for the *o*- and *m*-structures.

A series of preparative separations of stereoisomeric derivatives of 1,3-dioxolane was described by the present authors.[143] These five-membered cyclic acetals are of interest as model systems for the study of the stereochemistry of various natural physiologically active substances. Calculations of the thermodynamic parameters of solution[143] showed that the diastereoisomers of 2,4,5-tri-isopropyl-, 2-phenyl-4,5-di-isopropyl-, and 2-phenyl-2-methyl-4,5-di-isopropyl-1,3-dioxolanes, synthesised by the acid-catalysed condensation of *meso*- and *dl*-2,5-dimethylhexan-3,4-diols with the corresponding carbonyl compounds, have extremely similar properties. The similar di- and trialkyl(aryl)-derivatives of 1,3-dioxolane also have similar properties,[144–147] and this made it necessary to use preparative columns with lengths of 20 m and 7.5 m. Examples of the preparative CGC separation of 2-substituted 4,5-di-isopropyl-1,3-dioxolanes are shown in Fig.8. The separation was carried out on a circulation assembly with the valve switching system described in Ref.137. The separation factor for the *syn*- and *anti*-isomers of 2-phenyl-4,5-di-isopropyl-1,3-dioxolane, according to the analytical chromatogram, was 1.048. The efficiency of the preparative separation at the seventh half-cycle reached 14.5 thousand t.p. (with respect to the *syn*-isomer). The separation of the *syn*- and *anti*-isomers of 2,4,5-tri-isopropyl-1,3-dioxolane, for which the differences in the free energies of solution in the temperature range 110–140 °C do not exceed 38–55 J $mole^{-1}$ (that is $\alpha = 1.011$–1.019), required an efficiency of more than 50 thousand t.p.

In the experiments described above, the quantity of products being separated simultaneously was 0.5–1.0 g, which corresponds to the scale of the laboratory studies usually carried out in synthetic organic chemistry at the present time. CGC may also find extensive application, however, in special preparative studies involving the accumulation of large quantities of individual isomers for a more detailed study of their physicochemical properties, for use in subsequent synthetic studies, or for carrying out biological tests.

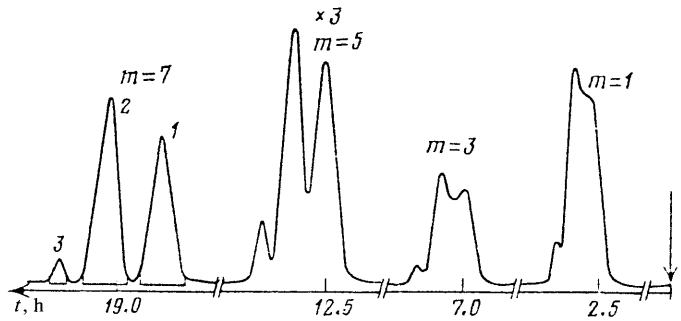


Figure 8. Fragments of the chromatogram of the preparative CGC separation of a mixture of *cis-anti*- (*1*), *cis-syn* (*2*), and *trans*-2-phenyl-4,5-di-isopropyl-1,3-dioxolanes (*3*) on 4 m × 23 mm columns filled with DC-550 polyphenylsiloxane oil (15%). Conditions: temperature of the columns 210 °C, p_{in} = 0.64 MPa, p_{out} = 0.59 MPa, carrier-gas (nitrogen) velocity 480 ml min^{-1}, removal of gas between columns 3.3%, original loading 0.6 ml, yield of separated products 79.5%.

The present authors used a semi-continuous version of highly efficient CGC to separate a mixture of the *cis*- and *trans*-isomers of 2,5-dimethyl-1,3-octathiane.[138] The preparative assembly operated at an inlet pressure of 0.59 MPa and an outlet pressure of 0.56 MPa, the quantity of carrier gas removed was 2%, the temperature of the columns 140 °C, the carrier-gas (nitrogen) velocity 300 ml min^{-1}, and the magnitude of the original specimen 0.65 ml. The stationary phase was Carbowax-20M (10%) in columns with dimensions 4 m × 23 mm. Beginning from the eighth half-cycle, when the band of chromatographic compounds had spread throughout the entire length of the column, the circulation was continued under non-pulse chromatographic conditions. The introduction of fresh portions of the mixture being separated and the removal of the enriched ends of the chromatographic band were carried out in each half-cycle in quantities of 50 μl. By the seventeenth half-cycle, ten additional quantities of the mixture had been introduced, and ~0.5 ml of separated products had been collected, corresponding to 43% of the total loading. Analysis of the collected fractions by capillary chromatography (column length 40 m, efficiency 70 thousand t.p. with respect to benzene) showed that the compounds were practically pure, containing not less than 99.6% of the individual components.

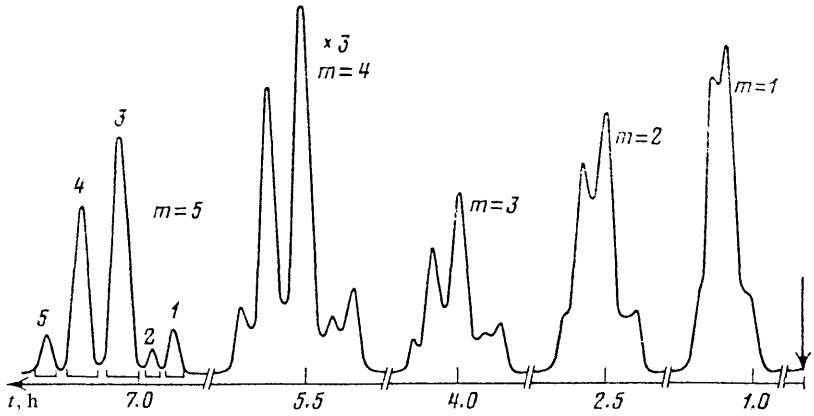


Figure 9. Fragments of the chromatogram of the preparative CGC separation of the high-boiling fraction of the distillate of the light oil, purified from phenol, of the tar from the semi-coking of Cheremkhovo coal on 4 m × 23 mm columns filled with DC-550 polyphenylsiloxane oil (15%). Conditions: temperature of columns 235 °C, p_{in} = 0.64 MPa, p_{out} = 0.58 MPa, carrier-gas (nitrogen) velocity 450 ml min^{-1}, removal of gas between columns 3.7%, original loading 0.5 ml; *1*) benzothiophene, *2*) methylbenzothiophene, *3*) β-methylnaphthalene, *4*) α-methylnaphthalene, *5*) biphenyl; efficiency of separation after the fifth half-cycle 12.5 thousand t.p. (with respect to β-methylnaphthalene); yield of separated products 84%.

Highly efficient preparative CGC has also been used to study the composition of various products of the treatment of coal. The importance of the complete and rational utilisation of the products of the processing of coal is making it necessary to develop accessible methods for separating and analysing the compounds originating from coal. The present authors and the Technological Laboratory of the Institute of Organic Chemistry of the Academy of Sciences of the USSR have studied the composition of the light oil, purified from phenol, with boiling point up to 250 °C, obtained as a fraction of the tar from the medium-temperature coking of coal from the Cheremkhovo deposit (Irkutsk coalfield).[138] The results obtained in the course of this study showed the promising possibilities provided by the use of preparative CGC at the stage involving the separation of the substances being studied from the semi-coking products. CGC showed that the light oil from the tar obtained in the medium-temperature coking of Cheremkhovo coal contains normal saturated, cyclic, and aromatic hydrocarbons, heterocyclic sulphur-containing compounds of the thiophene and benzothiophene series, and also condensed aromatic hydrocarbons, mainly of the naphthalene series. Fig.9 gives a chromatogram for the preparative separation of one of the narrow fractions of light oil from the tar obtained in the thermal degradation of Cheremkhovo coal.

Until recently, the separation of enantiomers of α-aminoacids by gas–liquid chromatography on optically active stationary phases was carried out using highly efficient capillary columns. Thanks to the availability of highly selective chiral liquid phases,[148] the number of which has increased considerably in recent years,[149–153] it has been possible to use for this purpose not only capillary columns but also fairly efficient short packed columns.[154–157] In this connection, promising possibilities are provided by the preparative separation of racemates using short packed columns with a selective chiral stationary phase included in a circulation scheme.

CGC has been used[158] to separate the enantiomers of alanine (Fig.10), valine, norvaline, leucine, norleucine, alloisoleucine, and isoleucine as the isopropyl esters of the N-trifluoroacetyl derivatives of N-stearyl-L-valine t-butylamide as liquid phase. The experiments were carried out as models for the subsequent preparative separation of the optically active compounds from the racemic mixtures, and it was shown[158] that the proposed chiral separating agent successfully combines a fairly high thermal stability (≧170 °C) with a high separating power. Even when the chiral diamide was mixed with achiral polyethylene glycol in the ratio 1:1, it was possible to achieve the practically complete separation of the enantiomers of a number of aminoacids.

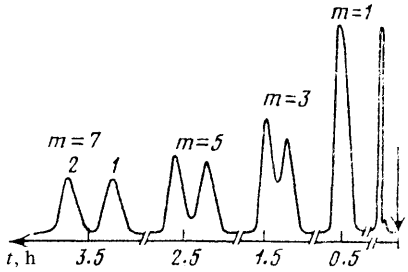


Figure 10. Fragments of the chromatogram of the CGC separation of the racemic isopropyl ester of N-trifluoroacetylalanine. Conditions: 2 m × 3 mm columns, N-stearyl-L-valine t-butylamide (4.6%) and PEG-20 M (4.4%) on N-Super Chromaton, temperature of columns 137 °C, p_{in} = 0.69 MPa, p_{out} = 0.65 MPa, carrier-gas (helium) velocity 35 ml min^{-1}, removal of gas between columns 2.5%, specimen volume 1 μl, *1* and *2*) *D*- and *L*-isomers respectively.

Subsequently, columns with dimensions 2.5 m × 8 mm with a sorbent containing 10% of the pure chiral stationary phase were used for the preparative separation of the racemates of a number of α-aminoacids.[159] Fig.11 gives fragments of t

chromatogram of the preparative separation of the racemate of norvaline by CGC. The optical purity of the separated enantiomers was followed from the dispersion of the optical rotation of the fractions collected and the pure *L*- or *D*-forms of the standard in solutions with similar concentrations, and it was shown that there was good agreement between the dispersion curves of the standard specimens and the corresponding separated fractions of the racemates, and also between the enantiomer pairs themselves. For a loading of the original racemate of 90–120 mg, the yield of the fractions separated, with allowance for the losses associated with the removal of part of the gas stream to achieve non-pulse chromatography conditions, is 70–90%. The productivity of the circulation assembly used, based on a standard LKhM-8MD gas chromatograph, corresponded to 0.4–0.6 g of racemate per day. A number of methods are available for increasing the productivity of the preparative separation of enantiomers, for example by the use of semi-continuous circulating systems. The above data make it possible to regard the preparative CGC of optically active substances as a new method for separating racemic mixtures, which has not been used before in organic chemistry and which may find a place in practical studies in fine organic synthesis and biochemistry.

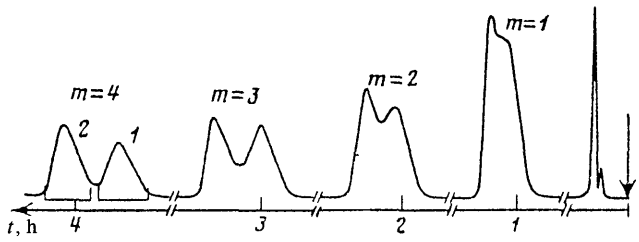


Figure 11. Fragments of the chromatogram of the preparative CGC separation of the racemic isopropyl ester of N-trifluoroacetylnorvaline on 2.5 m × 8 mm columns filled with N-stearyl-L-valine t-butylamide (10%) on Chromaton N-AW DMCS. Conditions: temperature of the columns 170 °C, p_{in} = 0.66 MPa, p_{out} = 0.60 MPa, carrier-gas (nitrogen) velocity 70 ml min^{-1}, removal of gas between columns 3.7%, original loading 90 mg; *1* and *2*) *D*(-) and *L*(+) isomers respectively; yield of separated products 90%.

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The ideas developed in the last ten years on the effects of the pulse contraction and broadening of chromatographic zones, the optimum conditions of non-pulse circulation chromatography established on this basis, and the new apparatus and procedures for carrying out circulation chromatography have laid the foundations for the use of this method for the highly efficient preparative separation of compounds with extremely similar properties.

Preparative circulation chromatography under non-pulse conditions, characterised by a linear increase in the number of theoretical plates with increase in the number of cycles, makes it possible to achieve an efficiency of separation comparable with that of capillary chromatography, using specimens which are larger by factors of 10^6–10^7. This makes it possible, within an acceptable time, to obtain the pure separated components in quantities sufficient for subsequent physical, chemical, and biological studies.

The extension of theoretical knowledge and the improvement of circulation techniques and procedures are opening up extensive possibilities for the further development of the circulation method in various forms of chromatography — gas, vapour-phase, liquid — as a method for the physicochemical study, analysis, accumulation, and preparative separation of compounds with similar structures and properties.

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